COMPARISION OF INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY

Dissertation submitted to

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In partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE

MADRAS MEDICAL COLLEGE

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CERTIFICATE

This is to certify that the dissertation titled, **"COMPARISION OF INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY"** submitted by **Dr. ARUNA.D** in partial fulfilment for the award of the degree of **DOCTOR OF MEDICINE in ANAESTHESIOLOGY** by The Tamilnadu Dr. M.G.R. Medical University, Chennai is a bonafide record of work done by her in the **INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE,** Madras Medical College, during the academic year **2016-2019.**

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CERTIFICATE OF THE GUIDE

This is to certify that the dissertation titled, **"COMPARISION OF INTRAVENOUS DEXMEDETOMIDINEAND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY"** is a bonafide research work done by **Dr.ARUNA.D** in partial fulfilment of the requirement for the degree of **DOCTOR OF MEDICINE IN ANAESTHESIOLOGY**, during the academic year 2016-2019.

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DECLARATION

I hereby declare that the dissertation titled, **"COMPARISION OF INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY"** has been prepared by me under the guidance of **Prof. Dr. SAMUEL PRABHAKARAN, M.D (ANAES),** Professor of Anaesthesiology, Institute of Anaesthesiology & Critical care, Madras Medical college, Chennai, in partial fulfilment of the regulations for the award of the degree of **M.D (Anaesthesiology)**, examination to be held in April 2019.

This study was conducted at Institute of Anaesthesiology& Critical care, Madras Medical College, Chennai. I have not submitted this dissertation previously to any journal or any university for the award of any degree or diploma.

Date:

Place: Chennai **DR.ARUNA.D**

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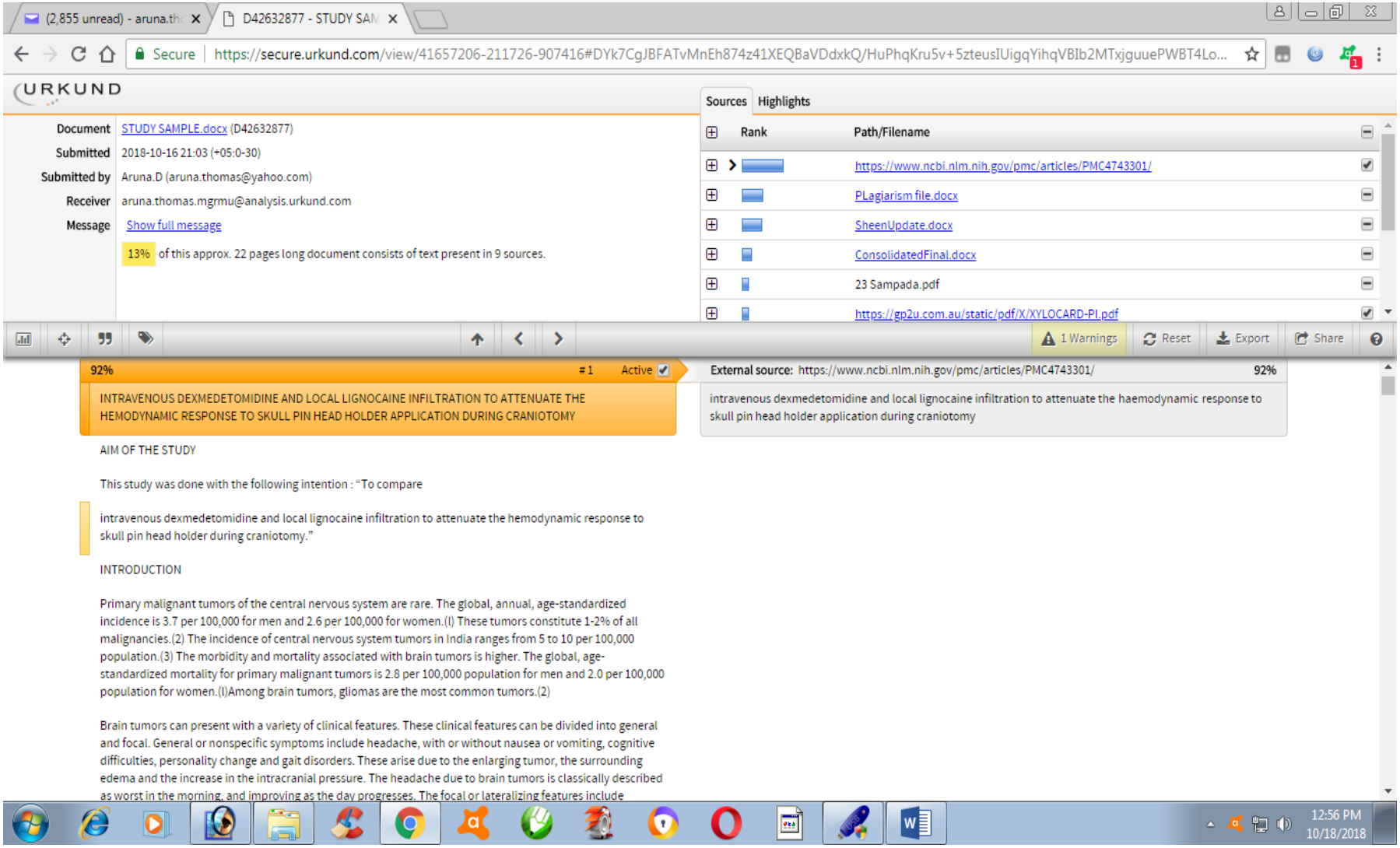
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INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY
AIM OF THE STUDY
This study was done with the following intention : "To compare
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INTRODUCTION
Primary malignant tumors of the central nervous system are rare. The global, annual, age-standardized incidence is 3.7 per 100,000 for men and 2.6 per 100,000 for women.(1) These tumors constitute 1-2% of all malignancies.(2) The incidence of central nervous system tumors in India ranges from 5 to 10 per 100,000 population.(3) The morbidity and mortality associated with brain tumors is higher. The global, age-standardized mortality for primary malignant tumors is 2.8 per 100,000 population for men and 2.0 per 100,000 population for women.(1)Among brain tumors, gliomas are the most common tumors.(2)
Brain tumors can present with a variety of clinical features. These clinical features can be divided into general and focal. General or nonspecific symptoms include headache, with or without nausea or vomiting, cognitive difficulties, personality change and gait disorders. These arise due to the enlarging tumor, the surrounding edema and the increase in the intracranial pressure. The headache due to brain tumors is classically described as worst in the morning, and improving as the day progresses. The focal or lateralizing features include
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PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"COMPARISION OF INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY"** of the candidate **Dr. ARUNA.D** with registration number **201620004** for the award of M.D., Degree in the branch of Anaesthesiology. I personally verified the urkund.com website for plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **13%** percentage of plagiarism in the dissertation.

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INTRODUCTION

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Primary malignant tumors of the central nervous system are rare. The global, annual, age-standardized incidence is 3.7 per 100,000 for men and 2.6 per 100,000 for women.[l] These tumors constitute 1-2% of all malignancies.[2] The incidence of central nervous system tumors in India ranges from 5 to 10 per 100,000 population.[3] The morbidity and mortality associated with brain tumors is higher. The global, age-standardized mortality for primary malignant tumors is 2.8 per 100,000 population for men and 2.0 per 100,000 population for women.(l)Among brain tumors, gliomas are the most common tumors.[2]

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The increase in intracranial pressure and the cerebral edema is of concern during the peri-operative period.

SKULL-PIN HEAD HOLDER:

The Mayfield skull-pin head holder is used to stabilize the head during neurosurgical procedures.

They support the head without any direct pressure on the face, allow access to the airway and hold the head firmly in one position that can be finely adjusted for optimal neurosurgical exposure.

Although it is an instrument of barbaric appearance, it is essential for operations in the sitting position and highly desirable for cervical or intracranial procedures in the prone or lateral position.

Different anaesthetic and pharmacologic technique, including local anaesthetic, narcotic, antihypertensive and deepening of anaesthesia with inhalation anaesthetics, have been used to blunt this deleterious effect with variable success.

When properly applied, the pins cause considerable periosteal stimulation. This results in abrupt increase BP and CBF under GA.

These hemodynamic responses may lead to brain edema, increase in ICP or ICH in aneurysm patients. Different anaesthetic techniques techniques have been used to blunt this deleterious effects with varaiable success.

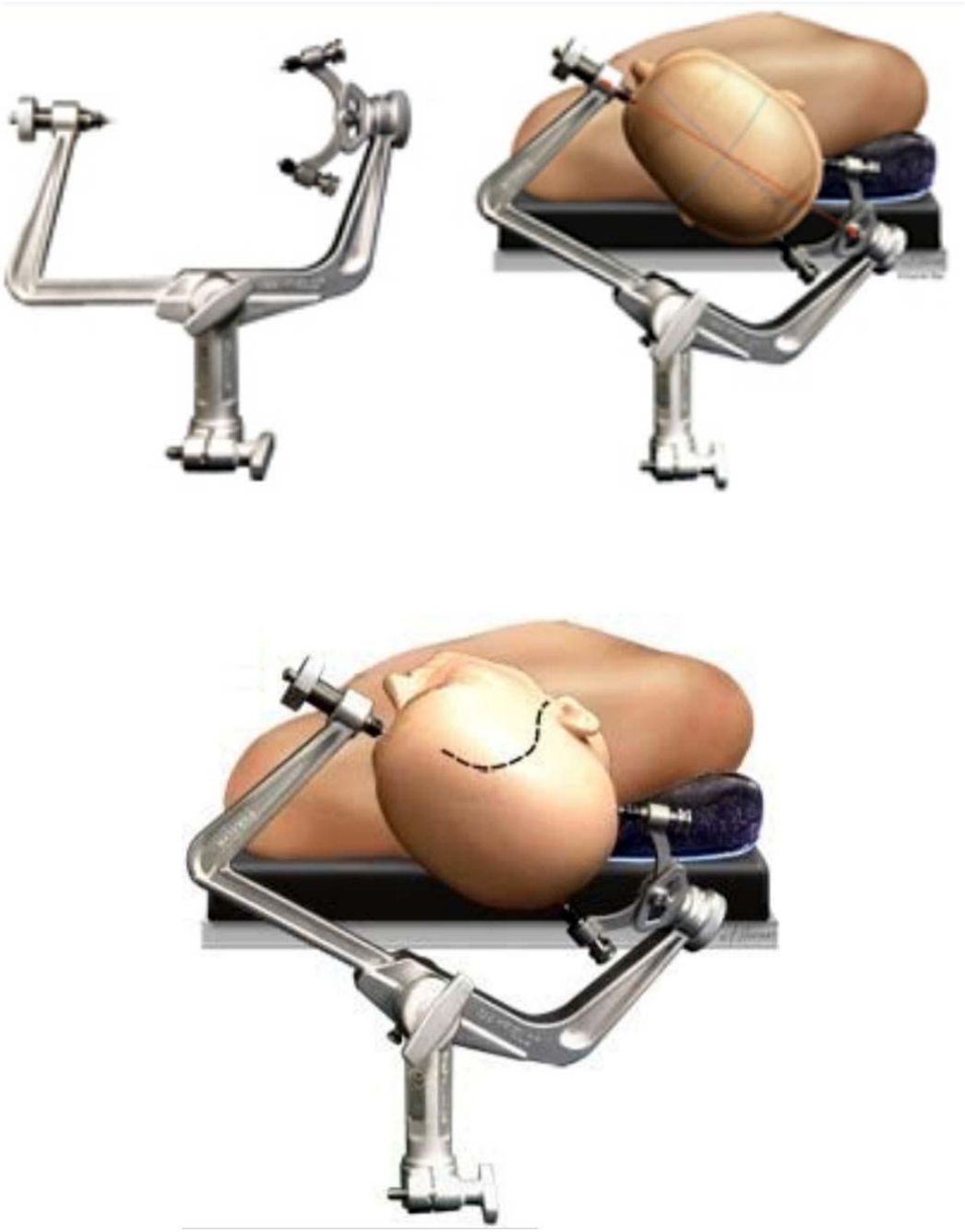
The stress response to intense nociceptive surgical stimulus is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system.

Attenuation of the cardiovascular and neuroendocrine responses to intense noxious stimuli during operation may improve outcome by beneficial effects on organ function.

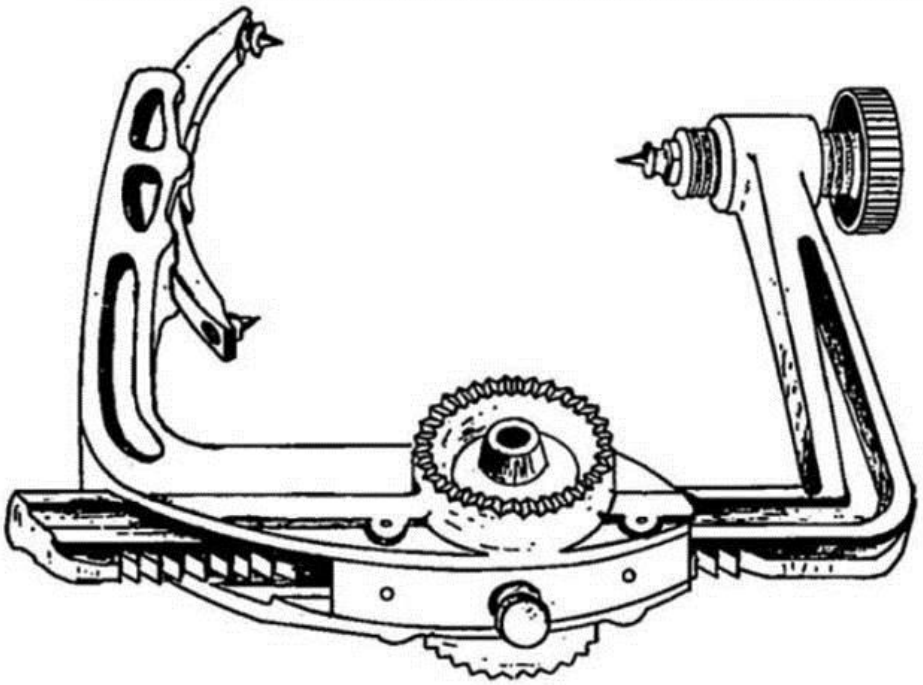
Dexmedetomidine is a highly specific potent and selective alpha-2 adrenoceptor agonist.It has sedative, analgesic and anaesthetic – sparing effects and it decreases HR,MAP and sympathetic nervous system activity in a dose dependent fashion.

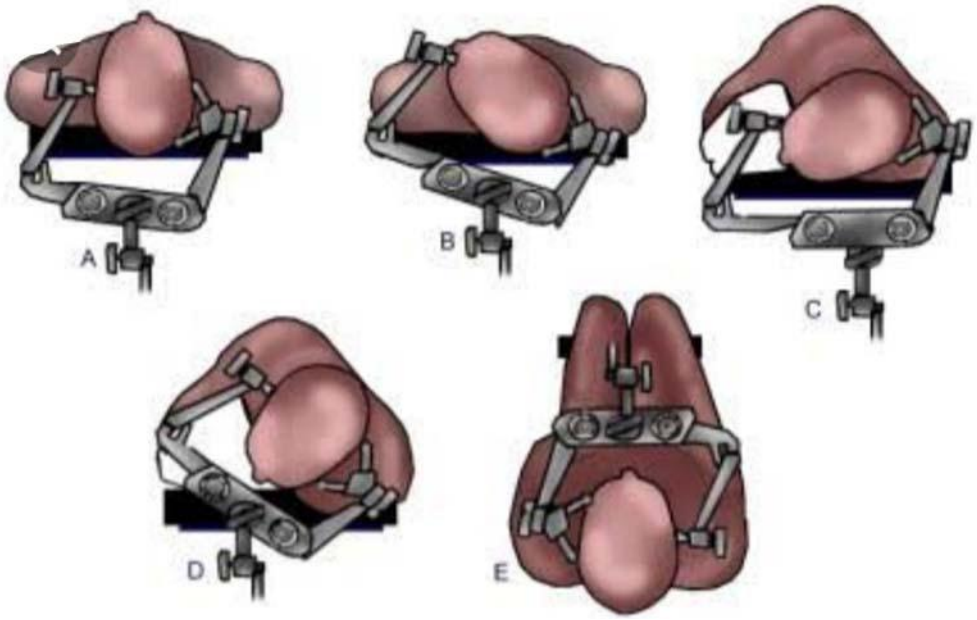
Lignocaine is a potent local anaesthetic that blocks the nerve conduction by decreasing the entry of sodium ions during upstroke of action potential. Lignocaine blocks sensory nerve endings, nerve trunks, neuromuscular junction, and ganglionic receptors. Autonomic fibers are generally more susceptible than somatic fibers.

In this prospective randomized study intravenous dexmedetomidine is compared with local lignocaine infiltration in attenuating the hemodynamic responses to skull pin head holder application during craniotomy.



MAYFIELD SKULL PIN HEAD HOLDER





DIFFERENT NEURO SURGICAL POSITIONS WITH THE AID OF SKULLPIN HEAD HOLDER

AIM OF THE STUDY

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NOXIOUS STIMULUS -

ITS RESPONSES

NOXIOUS STIMULUS - ITS RESPONSES

Prys-Roberts defined noxious stimulation as a mechanical, chemical, thermal, or radiation induced trespass causing potential or actual cell damage (fig. 1) shows the somatic and autonomic responses to noxious stimulation.

Noxious stimulation arises from somatic or visceral tissue and responses can be somatic or autonomic.

Somatic responses include both sensory and motor activity

Sensory response is perception of pain

A motor response is withdrawal of the stimulated part. This is the same concept that Eger and colleagues used more than four decades earlier when they defined the MAC as the drug concentration that blocked movement in response to noxious stimulation.

Prys - Roberts divided autonomic responses into four categories: breathing, haemodynamic, sudomotor and hormonal

HEMODYNAMIC RESPONSES

The hemodynamic response consists of autonomic responses to noxious stimuli, namely- increased sympathetic tone, which elevates blood pressure and the heart rate.

The sudomotor response consist of sweating, whereas the hormonal responses consist of catecholamine's and corticosteroids, Prys-Roberts considered pain relief, muscle relaxation and suppression of autonomic activity to be discrete pharmacologic effects. Some drugs can produce all these end points. Others produce only one or two.

STRESS RESPONSES

The stress responses was initially described by Hans selye as "the non- specific response of the body to any demand upon it"

The human body is an adaptable organism that has many interrelated mechanisms designed to identify, respond and neutralize both internal and external events that threatens or upsets homeostasis.

Anaesthesia and surgery involve manipulation of body physiology leading to activation of the body's responses to stress.

The stress response evolved as a mechanism for assisting the organism in reacting to immediate danger

Although once regarded positively as the body's defense mechanism. Today the stress response is regarded more equivocally since its physiologic consequences, especially increasing the output of various organ systems, may lead to increased morbidity and mortality by overtaxing already compromised organ system.

THE HYPOTHALAMIC PITUITARY AXIS:

The response to surgical and traumatic stress is triggered by hypothalamic activation secondary to afferent neuronal input from an area of injury such as inflammatory cytokines, TNF -a, IL-1 and IL6

Hypothalamic activation increases the activity of the sympathetic nervous system, which increases the output of the cardiovascular system, stimulates the adrenal medulla to secrete epinephrine and the pancreas to secrete glucagon

The endocrine system

The hypothalamic pituitary axis is the main controller of the endocrine system which in turn controls much of the body's metabolic functioning.

The endocrine hormones are major mediators of the metabolic response to stress. The hormones glucagon, Cortisol and catecholamine

oppose the effects of insulin on glucose and lipid metabolism and are thus called the counter regulatory hormones.

SYMPATHO ADRENERGIC SYSTEM

The sympathoadrenergic system composed of the sympathetic nervous system and adrenal gland, produces and secretes the catecholamines: norepinephrine epinephrine and dopamine.

Catecholamines have major effect on the cardiovascular system and also have major metabolic effect.

Glucagon- Insulin

Glucagon and insulin are both secreted by the pancreas, the former by the alpha cell, the later by the beta cells. The principal action of glucagon is to stimulate hepatic glycogenolysis and gluconeogenesis.

Serum glucagon concentration rises after most types of major surgery. The glucagon - insulin ratio increase because, insulin concentration decrease during surgery.

Glucocorticoid

Cortisol is a major stress hormone whose plasma levels are markedly elevated after surgical and traumatic stress. This is mainly due to enhanced secretion by the adrenal cortex.

In addition, this Cortisol production is minimally suppressed by exogenous glucocorticoid administration. This was demonstrated by the inability of 24 mg/day of dexamethasone administered for 2days after craniotomy to suppress the elevated concentration of either ACTH or Cortisol.

Cortisol is thought to cause insulin resistance by decreasing the rate of insulin activation of the glucose uptake system.

Cortisol is a vital mediator of stress because it facilitates catecholamine action and secretion, thus helping to maintain cardiovascular stability during surgical stress.

The counter regulatory hormones

The hormones, glucagon, catecholamine, and Cortisol are called counter regulator hormones because they oppose the effect of insulin and act synergistically to increase glucose production.

PROLACTIN

Prolactin release from the pituitary gland is a very sensitive marker of both physical and physiological stress in mammals.

The prolactin surge results from a general increase in the adrenergic activity in the hypothalamus. The stress induced prolactin release is a rapid, strong and transient response that can be evoked by large number of medical and surgical procedures.

METHODS TO ATTENUATE HEMODYNAMIC RESPONSES

METHODS TO ATTENUATE HEMODYNAMIC AND STRESS RESPONSES

Control of hemodynamic parameters during neurosurgical procedure is of great concern to the neuro-anaesthesiologist whose goals include optimal cerebral perfusion pressure.

Also, the balance of myocardial oxygen supply and demand must be preserved to minimize the risk of per-operative myocardial ischemia and infarction.

Factors affecting myocardial oxygen supply and demand Supply

1. Heart rate -diastolic time depends upon heart rate. Hence slower the heart rate, more the diastolic time and more the oxygen supply to the myocardium.
2. Coronary perfusion pressure - depends on aortic diastolic pressure and left ventricular end-diastolic pressure. It increases with a high aortic diastolic pressure and a low end diastolic pressure.
3. Arterial oxygen content - depends upon arterial oxygen tension and hemoglobin concentration.
4. Coronary vessel diameter.

Demand:

1. Basal requirement
2. Heart rate
3. Wall tension - preload, afterload
4. Contractility

A number of methods were used to attenuate cardiovascular response due to laryngoscopy and endotracheal intubation and skull pin placement

1. Deepening of general anesthesia

Inhalational agents - the deep level of anesthesia achieved by inhalational agents resulted in profound cardiovascular depression prior to skull pin placement

2. Lignocaine

Lignocaine has been demonstrated to produce intense analgesia when injected IV. Yukioka, et al demonstrated that the cough reflex was suppressed during intubation of trachea when plasma concentration of lignocaine was more than 2mcg/ml.

Levin R, et al demonstrated local mepivacaine infiltration safely protected against potentially dangerous increase in arterial pressure when the May field head holder was used

Mechanism

1. By increasing the depth of anesthesia
2. Potentiation of effect of N20 anesthesia and reduction of MAC of Volatile agents
3. Direct cardiac depression
4. Peripheral vasodilatation
5. Anti-arrythmic properties

3. Clonidine

It is an alpha 2 receptor agonist. Clonidine 4 to 5 mcg/kg orally 60 to 120 minutes prior to intubation or 1 to 3 mcg/kg intravenously immediate prior to intubation attenuates hemodynamic responses. Mechanism of action of alpha 2 agonist is decreasing central sympathetic out flow, increasing the parasympathetic tone and by decreasing circulating nor-adrenaline concentration.

4. Intravenous vasodilators

Hydralazine

Sodium nitroprusside

Nitroglycerin

5. Narcotics

Fentanyl	Morphine
Alfentanyl	Pethidine
Sufentanyl	Nalbhuphine

Fentanyl is the most commonly used narcotic agent. It is a potent analgesic, has a short duration of action, does not increase intracranial tension and has minimal circulatory changes.

6. Adrenergic blocker

Long acting: metoprolol, phentolamine, propranolol, labetalol, Short acting: esmolol

Of these, esmolol is the most commonly used agent because of its ultra short action.

It reduces heart rate, systolic blood pressure, ejection fraction and cardiac index but it maintains coronary perfusion pressure.

7. Calcium channel blockers

Nifedipine, nicardipine, verapamil, diltiazem Of these agents, nicardipine has got superior action.

8. Sedative and anxiolytics:

Midazolam and magnesium sulphate.

PHARMACOLOGY OF DRUG DEXMEDETOMIDINE

PHARMOCOLOGY OF THE STUDY DRUG DEXMEDETOMIDINE

Dexmedetomidine

It is a highly selective α2 - adrenergic agonist that produces sedation, hypnosis and analgesia.

History

The initiation for the use of α agonist in anesthesia resulted from observations made in patients during anesthesia who were receiving clonidine therapy. Dexmedetomidine was introduced in clinical practice in the United States in 1999. It was approved by FDA only as a short term (<24 hours) sedative for mechanically ventilated adult ICU patients.

Dexmedetomidine is now being used off-label outside of the ICU in various settings

Pharmacological profile

It is a highly selective α -adrenergic agonist. It shows a high ratio of specificity for the α receptor (all α \ 1600:1) compared with clonidine (all α2/ α1 200:1), making it a complete al agonist. Dexmedetomidine belongs to the imidazole subclass of al receptor agonists, similar to clonidine. It is freely soluble in water.

Metabolism and pharmacokinetics

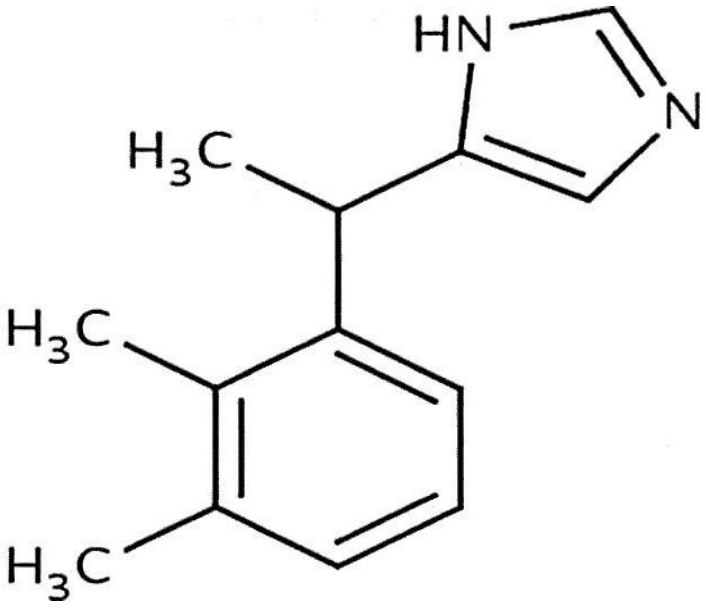
Dexmeditomidine has rapid redistribution half life -6min .Dexmedetomoidine is 94 % protein bound, and its concentration ratio between whole blood and plasma is 0.66. Metabolism: biotransformation by conjugation methylation (21%), or hydroxylation followed by conjugation in liver. The inactive metabolites are excreted in urine and feces. The elimination half-life of dexmedetomidine is 2-3 hours, with a context- sensitive half time ranging from 4 minutes after a 10 minute infusion to 250 minutes after an 8 hour infusion. No accumulation after infusions of 12-24 hrs duration.

Pharmacokinetics is similar in young adults and elderly.

Mechanism of actions

A selective α2-adrenoceptor agonist. Its action is unique and different. Three subtype of α2 adrenoreceptors have been described in humans: α2A, α2B and α2C.

Structural formula



α2A adrenoreceptors are primarily distributed in the periphery, whereas α2B and α2C are in the brain and spinal cord.

- Presynaptic activation of α2- adrenoreceptors inhibit the release of nor-epinephrine.
- Postsynaptic activation of αd- adrenoreceptors in the central nervous system inhibits sympathetic activity and can decrease blood pressure and heart rate, so sedation and anxiolysis can result from this activity.
- Analgesia is provided through binding of dexmedetomidine to α2 adrenoreceptors in the spinal cord.

The overall response to α2 adrenoreceptor agonist is related to the stimulation of α2 adrenoreceptor located in the central nervous system and spinal cord. The α2 agonists produce their sedative - hypnotic effect by an action on α2 receptor in the locus ceruleus and an analgesic action at α2 receptors within the locus ceruleus and within the spinal cord.

Action

Effect on central nervous system

Sedation

The α2 agonists act through the endogenous sleep- promoting pathways to exert their sedative effect.

It produces a unique sedative quality - **someone be clinically sedated yet arousable**

- Patient sedated, remaining so when unstimulated. but when stimulated they are arousable, alert, and able to respond without becoming uncomfortable
- It's also observed that they would quickly return to their sleep -like state.
- This characteristic allows for "daily wake up" tests to be done in a safe fashion.

- Despite sound levels of sedation with dexmedetomidine, there is limited respiratory depression, providing wide safety margins.

Analgesia

The analgesic effects of dexmedetomidine are complex. α2 agonists do have an analgesic effect when injected via the intrathecal or epidural route. The primary site of analgesic action is thought to be the spinal cord.

Systemic use of dexmedetomidine shows narcotic sparing. In the postoperative ICU setting, narcotic requirements were reduced by 50% when patients were receiving dexmedetomidine.

In human pain studies, the results of systemically administered dexmedetomidine are inconsistent. Modest reductions in pain was observed.

In the clinical setting, when pain is likely to occur, if dexmedetomidine is to be used, the addition of a narcotic seems warranted.

Other central nervous system effects

Dexmedetomidine in animal models of incomplete cerebral ischemia and reperfusion reduces cerebral necrosis and improves neurologic outcome by reducing the intracerebral catecholamine outflow and the reduction of the excitatory neurotransmitter glutamate during injury.

Dexmedetomidine also is able to reduce muscle rigidity after high-dose opioid administration.

Effects on the respiratory system

Dexmedetomidine at concentrations producing significant sedation reduces minute ventilation, but retains the hypercapnic ventilatory response. The changes in ventilation appeared similar to those observed during natural sleep. Dexmedetomidine has been implicated in blocking histamine-induced bronchoconstriction in dogs.

Effects on cardiovascular system

The basic effects of α2 agonist on the cardiovascular system are decreased heart rate, decreased systemic vascular resistance and indirectly decreased myocardial contractility, cardiac output, and systemic blood pressure.

The hemodynamic effects of a bolus of dexmedetomidine in humans have show a biphasic response- an initial increase in blood pressure (22%) and decrease in heart rate (27%) from baseline that occurred at 5 minutes after injection (probably due to the vasoconstrictive effects of dexmedetomidine when stimulating peripheral od receptors) followed by

heart rate return to base line by 15 minutes, and blood pressure decrease 15% below base line by 1 hour.

The incidence of hypotension and bradycardia may be related to the administration of a loading dose. Omitting the loading dose or not giving more than 0.4ug/kg reduces the incidence of hypotension. Giving the loading dose over 20 minutes also minimizes the transient hypertension.

Dosage and administration

- Dexmedetomidine is supplied in a 2-ml ampoule, 100 mcg/ml.
- Dexmedetomidine must be diluted in 0.9% sodium chloride to achieve the required concentrations prior to administration. To prepare the infusion, withdraw 2ml of dexmedetomidine and add to 48 ml of 0.9% sodium chloride injection to total of 50 ml.
- The target concentration is 4mcg/ml. so 2ml of dexmedetomidine needs to be diluted to 50 ml in 0.9% sodium chloride.
- Loading dose - 0.5µg - lµg/kg (6-12ml) over 10 min [36-72ml/hr]
- Maintenance -0.3µg - 0.7µg / kg / hr (4-9ml/hr)
- Titration ± 0.1µg/kg/hr- 1.25 ml/hr Uses

Dexmedetomidine has been approved as a short term sedative for adult intubated patients in ICU. Given its well - documented beneficial effects of anxiolysis, sedation, analgesia, and sympatholysis with minimal respiratory depression, it also has been used in various other clinical scenarios .

1. Intensive care unit

Dexmedetomidine has following advantages for sedation in mechanically ventilated postoperative patients.

- Decreased requirement for opioids (>50%) when Dexmedetomidine is used for sedation compared with propofol or benzodiazepines.
- The PaO2/ FiO2 ratio was significantly higher in the Dexmedetomidine group
- Providing adequate sedation with minimal respiratory depression -can be used when weaning patients from the ventilator.

α2 adrenoreceptor agonists have been used in the treatment of alcohol and drug withdrawal of narcotics, benzodiazepines, alcohol, and recreational drugs.

2. Anesthesia

a) Dexmedetomidine at IV doses of 0.33 to 0.67 ug/kg given 15 minutes before surgery attenuates the hemodynamic response to endotracheal intubation.

b) As a premedicant IM injection (2.5µg/kg)

c) Dexmedetomidine is used as a premedication 10 minutes before general surgery for cataract removal. Intra ocular pressure is decreased (33%) catecholamine secretion is reduced, perioperative analgesic requirements are less and recovery is very rapid

d) Dexmedetomidine is used for securing the airway with a fiberoptic intubation

e) Dexmedetomidine has been used for sedation for monitored anesthesia care in gynecological, urological, burns patients, trauma patients, and pediatric patients and in obese, OSA patients.

f) Sedation during regional anesthesia.

g) Dexmedetomidine is also useful as anesthetic adjuvant in Bariatric surgery, sleep-apnea patients, craniotomy aneurysm, AVM [hypothermia], cervical spine surgery, off pump CABG, vascular surgery, thoracic surgery, injury, burns, trauma, alcohol withdrawal.

Contraindications

- Infusion over 24 hours
- In obstetric procedures, caesarean section deliveries, the safety has not been studied.
- Patients with pre-existent severe bradycardia and related bradydysrhythmias (e.g., advanced heart block)
- Patients with impaired ventricular function (ejection fraction <30%)
- Patients who are hypovolemic or hypotensive.
- Patients with raised intracranial tension

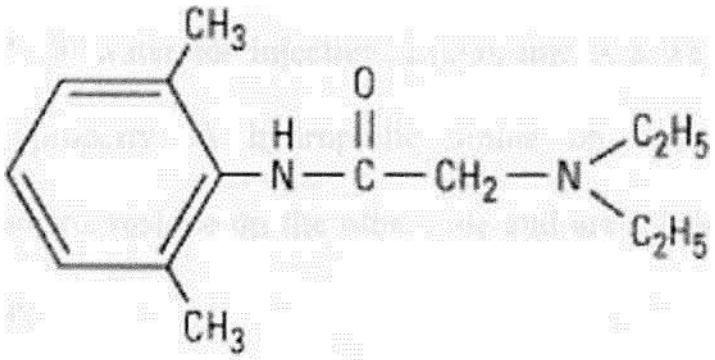
Antidote

All effects of Dexmedetomidine could be antagonized easily by administering the alpha 2 - adrenoceptor antagonist atipamezole (A-17)

PHARMOCOLOGY OF DRUG

LIGNOCAINE

PHARMACOLOGY OF LIGNOCAINE



Lidocaine

Lignocaine was synthesized in 1943 in Sweden by Lofgren and was introduced into clinical practice in 1948.

DESCRIPTION

Lignocaine hydrochloride is 2-diethylamino-aceto-2'6xylilide hydrochloride monohydrate. It appears as a white, odourless crystalline powder. It is very soluble in water, freely soluble in chloroform and in ethanol .It is practically insoluble in ether.

Molecular formula - C14H22 N20 Hcl.H20

Molecular weight - 288.8

Lignocaine hydrochloride injection is an isotonic, sterile solution containing Lignocaine hydrochloride B.P., 1% or 2%, and sodium chloride, B.P., in water for injection. Lignocaine is a weak base with amphiphillic property. A hydrophilic amine on one side and a lipophillicaromatic residue on the other side and are joined through an amide linkage.

MECHANISM OF ACTION:

Local anesthetics block the nerve conduction by decreasing the entry of sodium ions during upstroke of action potential. As the concentration of local anaesthetic is increased the rate of rise of action potential and maximum depolarization decreases causing slowing of conduction. Finally local depolarization fails to reach the threshold potential and conduction block ensues. The local anesthetics interact with a receptor situated within the voltage sensitive sodium channel and raise the threshold of channel opening.

Sodium channel has an activation gate (A) near its extracellular mouth and an inactivation gate (I) at the intracellular mouth. In the resting state, the activation gate is closed. Threshold depolarization of the membrane opens the activation gate allowing sodium ions to flow in along the concentration gradient. Within a few milliseconds inactivation gate closes and ion flow ceases.

The local anesthetic receptor is located within the channel in its intracellular half. Local anesthetic traverses the membrane in its lipophillic form (B+), reionises in the axoplasm and approaches the LA receptor through the intracellular mouth of the channel. It is the cationic form of local anesthetic (BH+), which primarily binds to the LA receptor. The receptor has higher affinity or is more accessible to local anesthetic in the activated state compared to the resting state. Binding of LA to its receptor stabilizes the channel in the inactive state and thus reduces the probability of channel opening.

Action of receptors within the sodium channel accounts for 90% of nerve blocking effect. Nonspecific membrane expansion accounts for the remaining 10% of the action and is analogous to the electrical stabilization produced by a number of non-polar, purely lipid solvable substances such as barbiturates, general anesthetics and Benzocaine.

PHARMACOLOGICAL ACTION:

LOCAL - Minimal local irritant action and blocks sensory nerve endings, nerve trunks, neuromuscular junction, and ganglionic receptors.

REGIONAL - Autonomic fibers are generally more susceptible than somatic fibers. Among the somatic afferents, the order of blockade is pain, temperature, touch, deep pressure.

SYSTEMIC - Effect is mainly on CVS or CNS.

CVS: In cardiac tissue, a therapeutic serum concentration (1.5 to 6. micrograms / ml) of Lignocaine will produce the following effects:

Depression of slow spontaneous depolarization (phase 4), that is the automaticity of isolated, non-polarised purkinje fibres, while having little effect on membrane responsiveness, conduction velocity, or cardiac output. Automaticity due to stretch, hypoxia or catecholamine's can also be suppressed by Lignocaine.

Shortening of action potential period and effective refractory period of purkinje and ventricular cells.

Thus it has a stabilizing effect on cell membrane of cardiac tissue. It also stabilizes aberrant conduction.

CNS: Low plasma concentration of LA is likely to produce numbness of tongue and circumoral tissues. As plasma concentration increases it crosses blood-brain-barrier and produces restlessness, vertigo, tinnitus and difficulty in focusing. Then slurred speech and skeletal muscle twitching occur. Lignocaine causes drowsiness before seizures. Seizures are classically followed by CNS depression, which may be accompanied by hypotension and apnea.

PHARMACOKINETICS

Following IV injection, the blood level of Lignocaine declines due to rapid distribution into various tissues including the heart, with a half-life of 7 to l0mins, within the first hour. After this initial phase, the half-life is 90 to 120mins (metabolism and excretion). Absorption is slow in regional anesthesia.

METABOLISM AND EXCRETION

The principle metabolic pathway of Lignocaine is oxidative dealkylation in the liver to monoethylglycinexylidine following by hydrolysis of this metabolite to xylidine. Monoethylglycinexylidine has approximately 80% of the activity of Lignocaine for protecting against cardiac dysrhythmias. This metabolite has a prolonged elimination half time. Xylidine has approximately 10% of the activity of Lignocaine.

Hepatic disease or decrease in hepatic flow, which may occur during general anesthesia, decreases the rate of metabolism of Lignocaine. Excretion is through the kidneys. Approximately 90% of the dose is excreted as metabolites and less than 10% is excreted unchanged in the urine.

DOSAGE

For regional anesthesia: 3mg/kg, with adrenaline 7mg/kg. For cardiac arrhythmias, therapeutic serum concentration of Lignocaine is 5 to 20micromol/L or 1.5 to 6.0 micrograms/ ml. In order to obtain therapeutic blood levels rapidly, a single intravenous dose of lmg/kg should be given over 1 to 2 minutes. The initial effect will occur in 2 to 4 minutes, and may last as long as 20 minutes.

This should be followed within 10 minutes, by a continuous infusion at the rate of 2 to 4 mgs/min. In order to maintain therapeutic blood levels, the initial dose may be repeated by two more injections at 15 to 20 min intervals but it should not exceed 300mg of Lignocaine within a 1 hour period. Since it has a very narrow therapeutic window, infusion should be promptly stopped when there is an undue prolongation of PR interval or QRS complex .To attenuate the cardiovascular stress response to intubation, Lignocaine 1.5mg/kg IV 3 min prior to laryngoscope should be given.

ADVERSE EFFECTS /TOXICITY:

Due to high plasma levels as a result of excessive dosage, rapid absorption, delayed elimination or inadvertent IM injection during local anesthetic use.

CNS: Lightheadedness, drowsiness, disorientation, confusion, nervousness, agitation, psychosis, euphoria, tinnitus, blurred vision, slurred speech, numbness, twitching, tremors, convulsions, unconsciousness, seizures, coma, respiratory depression and arrest.

CVS: Hypotension, bradycardia, arrhythmias, heart block and CVS collapse which may lead to cardiac arrest. Meth-hemoglobineamia may occur following IV administration.

HYPERSENSITIVITY:

Rare with Lignocaine.

NEUROLOGICAL SYSTEM:

Persistent anesthesia, paresthesia, weakness, paraplegia of lower extremities and loss of sphincter control mav occur.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1. Tim G Costello et al had done a study comparing hemodynamic responses to intubation and pin head holder application in two groups of neuro surgical patients given oral clonidine (3mg/kg) or oral Temazepam (10-20mg), 90 min before induction of anesthesia.

Mean arterial blood pressure (MAP) and heart rate were recorded before the induction of anesthesia and before and after intubation and application of the pin head holder. Interventions required to maintain hemodynamic stability were compared between groups. Pre induction sedation stores and MAP values were similar between groups. MAP was significantly lower (p=0.031) in the clonidine group after pin head holder application. The study was concluded by observing that clonidine was effective in reducing the MAP increase with pin head holder application in neurosurgical patients.

2. Menda F et al had conducted a study in which dexmedetomidine was compared with placebo or attenuate hemodynamic response to endotracheal intubation in patients undergoing fast track CABG.

50 patients who were receiving Beta- blocker treatment were given dexmedetomidine (lmcg/kg) or placebo before induction of anesthesia. Heart rate (HR) and blood pressure (BP) were monitored at baseline, after placebo on dexmedetomidine infusion, after induction of anesthesia and at one, three, and five minutes after endotracheal intubation.

In the dexmedetomidine group systolic (SAP), diastolic (DAP) and mean arterial pressure (MAP) were lower at all times in comparison to baseline values. In the placebo group SAP, DAP and MAP decreased after the induction of general anesthesia and five minutes after the intubation compared to baseline values. This decrease was not significantly different between the groups.

After the induction the drop in HR was higher in DEX group compared to PLA group. One minute after intubation, HR significantly increased in PLA group while, it decreased in the DEX group. The study was concluded by observing that dexmedetomidine can safely be used to attenuate the hemodynamic response to endotracheal intubation in patients undergoing myocardial revascularization receiving /3- blockers.

3. Uyar, Yagmurdur et al had done a study in which dexmedetomidine was compared with a placebo to attenuate the hemodynamic and neuro endocrinal responses to skull pin head holder application during craniotomy patients. In this study, 40 patients undergoing craniotomy with attachment of a pin holder were randomly assigned to one of two equal groups. The placebo group received saline, where as the treatment group (DEX group) received a single bolus of dexmedetomidine (lmcg/kg)., intravenously over 10 minutes before induction of anesthesia. Arterial blood pressure, heart rate and sequential concentrations of circulating Cortisol, prolactin and blood glucose were measured. Relative to baseline and the other group, arterial blood pressure and heart rate decreased significantly after the administration of dexmedetomidine through skull pinning ($P<0.05$).

In both the groups plasma Cortisol, prolactin and blood glucose increased significantly relative to baseline and after skull pin insertion. However the values were significantly increased in the placebo group compared with the DEX group. The results suggested that a single bolus dose of dexmedetomidine before induction of anesthesia attenuated the hemodynamic and neuroendocrinal responses to skull pin insertion in patients undergoing craniotomy.

4. Jellish W,et al conducted a study in which effects of clonidine premedication and scalp infiltration of lidocaine on hemodynamic responses to laryngoscopy and skull pin head holder insertion were compared during skull base procedures. 34 patients undergoing skull base procedures were randomized to four groups. Group 1 received oral clonidine 5mcg/kg before surgery with 10-15 ml of 1% Lidocaine infiltrated at pin insertion sites. Group 2 received clonidine with saline infiltration. Group 3 received a placebo preoperatively and had lidocaine infiltrated at pin sites. Group 4 received a placebo and saline infiltration at pin insertion sites.

They concluded that clonidine attenuated HR increases after laryngoscopy, but not after H-H placement. Lidocaine injected at the pin sites reduced HR but MAP increased after H-H insertion. The combination of oral clonidine and scalp lidocaine blunted hemodynamic responses to both intubation and H-H placement

5. Scheinin et al conducted a study where IV dexmedetomidine was compared with a placebo to attenuate the sympathoadrenal responses to tracheal intubation

They studied in 24 ASA I patients, where either dexmedetomidine 0.6mcg/kg or saline was given I. V, 10 minutes before induction of anesthesia. They found that the required dose of thiopentone was significantly smaller ($p<0.001$) in the dexmedetomidine groups than in the control group and the drug attenuated the cardiovascular responses to laryngoscopy and tracheal intubation.

They concluded that dexmedetomidine attenuated the sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and pre operative fentanyl.

The stress response to laryngoscopy and endotracheal intubation activates the sympathetic nervous system, which may increase the myocardial oxygen demand by increasing HR and arterial blood pressure.

Of the various methods, high dose opioids may completely inhibit the stress response . These high doses of opioids are impractical.

6. Mollick MT, et al in a study used low dose of lignocaine or low dose of opioids and observed the cardiovascular response after laryngoscopy and endotracheal intubation. They used 100 patients of both sexes.

The cardiovascular parameters observed were HR,(SBP,) systolic blood pressure , diastolic blood pressure (DBP), and rate pressure product(RPP). Group 1 received lignocaine(lmg/kg) 2 minutes before induction of anesthesia.

Group II received inj. Pethidine lmg/kg and inj. Lignocaine lmg/kg intra venously . They concluded the study by observing that intravenous lignocaine with pethidine did attenuate the sympathetic responses to laryngoscopy and endo tracheal intubation.

7. Dobblar DD, et al compared four techniques for preventing or blocking the hypertensive responses to the insertion of Mayfield headrest skull pin. Intravenous alfentanil, IV esmolol, IV thiopental sodium and local anesthesia using plain lidocaine.

Of the 40 patients undergoing intracranial surgery requiring the use of May field headrest skull pin, 20 min after anesthetic induction and 2-3 minutes prior to insertion of head rest skull pin, one of these three drugs was administered IV. (Alfentanil 10 mcg/kg, esmolol lmg/kg or thiopental l.5mg/kg). The fourth drug lignocaine was administered by injection into the scalp.

Blood pressure, heart rate were recorded immediately prior to and after pin insertion with balanced general anesthesia.

This study was concluded by observing that IV alfentanil and local injection of xylocaine in the scalp prevented the hemodynamic response to the insertion of skull pins. Neither esmolol nor thiopentone prevented the hypertensive response. They further concluded that the rapid onset and short half life of alfentanil , coupled with the absence of hemodynamic effects at the dose used is an alternative to the use of lidocaine injection.

8. Kenya ,et al conducted a study in which the efficacy of dexmedetomidine in attenuating the sympathoadrenal responses to tracheal intubation and also analyzed reduction in intra -operative anesthesia requirement.

Sixty patients scheduled for elective surgery of more than 3 hours were randomly selected .Control group received isoflurane-opioid and study group received isoflurane opioid- dexmedetomidine anesthesia given over 10 min before induction of anesthesia and continued in a dose of 0.2-0.7 mcg/kg/hr until skin closure. All patients were induced with thiopentone fentanyl and vecuronium. Hemodynamic variables were continuously recorded.

The study resulted in observing that in the dexmedetomidine group , the need for thiopentone and isoflurane was decreased by 30% and 32% respectively. The conclusion of the study was that perioperative infusion of dexmedetomidine is effective in attenuating sympathoadrenal responses to tracheal intubation. They also concluded that dexmedetomidine has significant anesthetic and opioid sparing effect.

Tanskanen PE, et al conducted a randomized double blind study in which dexmedetomidine was used as an adjuvant in patients undergoing intracranial tumor surgery. In that study, it was concluded that there was an increased perioperative hemodynamic stability in patients undergoing brain tumor surgery without postoperative respiratory depression.

10. Bloor BC, et al conducted a study on the effects of intravenous dexmedetomidine in humans II Hemodynamic changes.

Here, they examined the hemodynamic effects of four selected IV doses in consenting healthy male volunteers. In a randomized trial subjects received 0(n=9), 0.25(n=6), 0.5(n=6), 1.0(n=6) or 2.0(n=10) mcg/kg of dexmedetomidine by infusion.

ECG, heart rate (HR), arterial blood pressure (MABP), bioimpedence cardiac output (CO) and plasma catecholamine concentration (CA) were monitored from 90 min before to 360 min after infusion. Plasma dexmedetomidine concentrations were measured.

The study was concluded thus: Even the lowest dose decrease CA (catecholamines) immediately to values close to 20PCG/ml for 5 hrs and 2min IV infusion of dexmedetomidine produced a transient increase in MABP and a longer lasting decrease in MABP and catecholamines.

MATERIALS & METHODS

MATERIALS AND METHODS

This study was conducted after obtaining approval from the institute ethical committee and patients' consent. Surgeon was informed of the study.

Study Design

Prospective Randomised Comparitive Study.

Patient selection

Age group: 18 – 70years

Sixty consecutive ASA I and II patients aged between 18 years and 70 years old , undergoing elective craniotomy for resection of supratentorial tumors with aid of skull pin head holder were randomized by closed envelope method into 2 groups.

This study was done during the period from July 2017 to September 2017 in the department of Anaesthesia, RGGGH, Chennai 3.

Exclusion Criteria

a. Hypertension
b. Ischaemic Heart Disease
c. Heart Block
d. Pregnancy or Lactation
e. Signs and Symptoms of raised intracranial pressures

f. previous craniotomy

g. Tumors of Hypophysis

h. Head injury

i. Patients not willing to participate in the study.

Materials

1. 18 G venflon
2. Drugs - Dexmedetomidine, 2%Lignocaine
3. 3.Drugs for general anaesthesia – Glycopyrrolate, Fentanyl, Propofol, Atracurium
4. Monitors – NIBP,ECG,SPO2,EtCO2.

METHODOLOGY

HEMODYNAMIC MEASUREMENT

Statistical Analysis

- Results for parametric data were reported as means ± SD
- Demographic parameter data were analysed by student ‘t’ tests.
- Non parametric data were analysed using x^2 test.
- Hemodynamic data were analysed by the independent ‘t’ tests for differences between group and paired “t” test for differences within groups.
- For post-hoc comparision , Bonferroni test was applied.
- A value of <0.05 was considered as statistically significant.

METHODOLOGY

ETHICAL COMMITTEE APPROVAL

⇩

PATIENT SATISFYING INCLUSION CRITERIA

⇩

INFORMED CONSENT OBTAINED

⇩

RANDOMIZATION BY CLOSED ENVELOPE METHOD

⇩

PRE- INDUCTION BASELINE
(HR, MAP MEASUREMENT, T1)

⇩

PRE-OXYGENATION

⇩

INDUCTION

⇩

INTUBATION WITH ENDOTRACHEAL TUBE

⇩

PRE-INFILTRATION VALUES T2

⇩

INFILTRATION WITH LOCAL LIGNOCAINE (GROUP-2)/
IV DEXMEDETOMIDINE (GROUP -1)

⇩

POST INFILTRATION VALUES (T3)

⇩

PRE-PIN APPLICATION (T4)

⇩

POST-PIN APPLICATION (T5)

⇩

10 MINUTE AFTER PIN APPLICATION (T10)

⇩

15 MINUTE AFTER PIN APPLICATION (T15)

⇩

SURGERY PROCEEDED WITH MAINTENANCE OF ANAESTHESIA

⇩

END OF SURGERY

⇩

EXTUBATION

⇩

DATA COMPILATION

⇩

STATISTICAL ANALYSIS

⇩

CONCLUSION

OUTCOME MEASURES

Heart Rate (HR) and Mean Arterial Pressure (MAP) were recorded at the following time intervals.

- Pre- induction baseline (immediately before IV administration of dexmedetomidine)
- Pre-infiltration (just before infiltration of pin sites)
- Post- infiltration (just after infiltration of all pin sites)
- Pre-pin application (just before pin application)
- Post-pin application

at T1, T 2, T 3, T 4, T 5, T 10 and T15 minutes respectively after Pin insertion

EVENTS	HEART RATE (HR)	NIBP	MEAN ARTERIAL PRESSURE (MAP)
Pre- induction baseline (T1)			
Pre-infiltration (T2)			
Post- infiltration (T3)			
Pre-pin application (T4)			
Post-pin application (T5)			
10 Minutes after pin application ((T10)			
15 Minutes after pin application (T15)			

OBSERVATION RESULTS AND ANALYSIS

OBSERVATION RESULTS AND ANALYSIS

Study Groups

Study Groups	Dexmedetomidine Group	Lignocaine Group	Total
Number	30	30	60
Percentage	50.00	50.00	100

DATA ANALYSIS

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test.. Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

Study

The efficacy of intravenous dexmedetomidine versus local lignocaine infiltration in attenuating hemodynamic response to skull pin head holder during craniotomy.

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In this study, Dexmedetomidine and Lignocaine significantly attenuated hemodynamic responses to skull-pin head holder with Dexmedetomidine being associated with incidence of hypotension and bradycardia.

Sample Size Calculation

Sample size was determined based on

Description:

The formula for determining sample size is given as:

$$n = \left(\frac{Z_{\alpha/2} \cdot \sigma}{E}\right)^2$$

Where

n = Sample size

σ = Population standard deviation

e = Margin of error

Z = The value for the given confidence interval

- The confidence level is estimated at 95%
- Standard deviation 13
- With a z value of 1.96
- The confidence interval or margin of error is estimated at +/- 3.5
- **Assuming that 80 percent as power of the study, minimum sample size required for the study was calculated to be 53**

Taking into account 10% attrition rate = 53+6=59

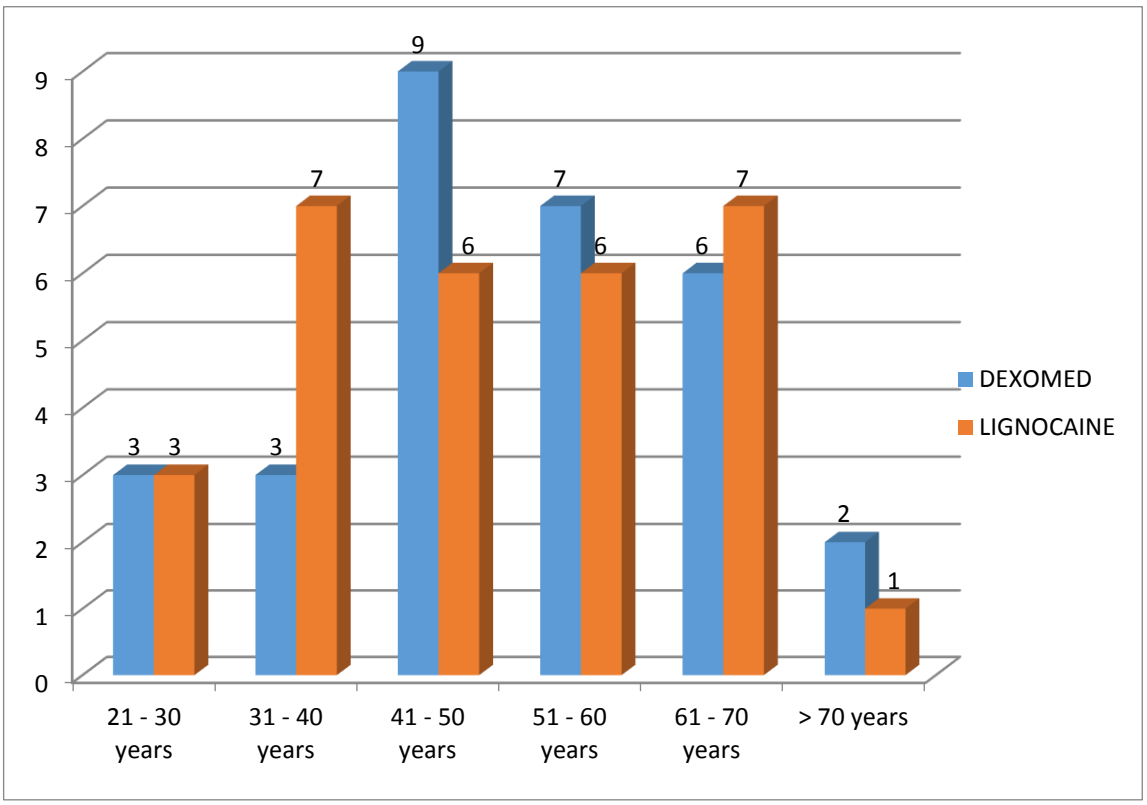
Thus 60 subjects will be chosen in our study.

Group Dexmedetomidine = 30

Group Lignocaine= 30

AGE

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
AGE	DEXOMED	30	51.23	13.91	0.442
	LIGNOCAINE	30	48.43	14.10	



Results

While analysing age distribution among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull pin head holder,it was observed that majority of the study subjects in Dexmed group were distributed inn 41-50 years age class interval(n=9) and between 31-40 years & 61-70 years age class interval(n=6) in Lignocaine group. (p=0.442, unpaired t test)

Discussion

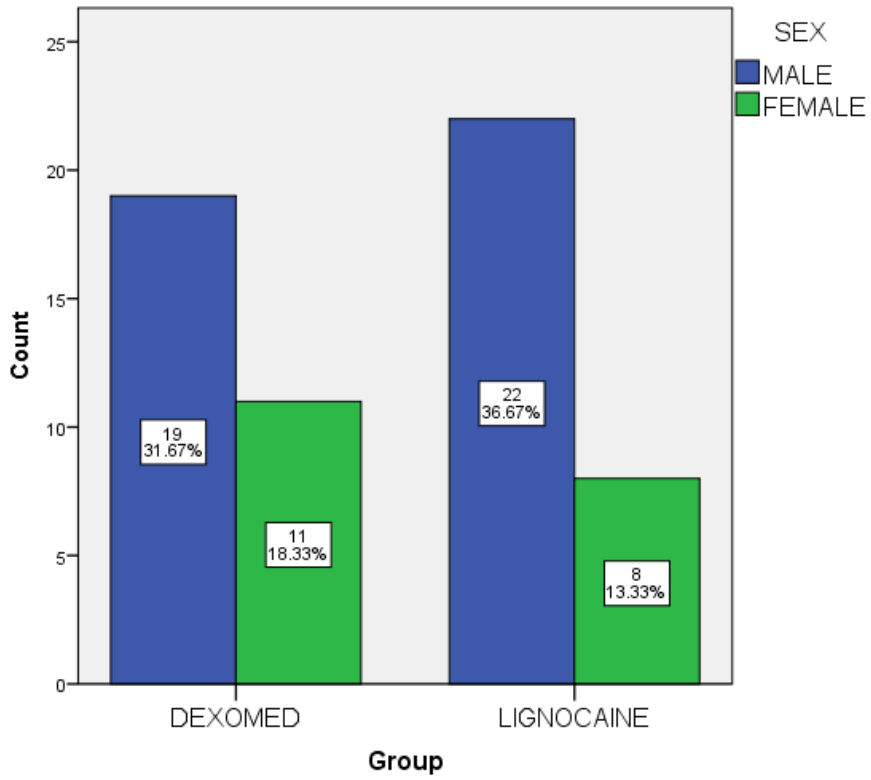
When statistically comparing age distribution between the intervention groups, the difference in the mean age of patients in dexmedetomidine group (51.23) and lignocaine group (48.43) was found to be statistically insignificant (p >0.05).

Conclusion

Age of the study subjects is normally distributed across the intervention groups and has no effect on study outcomes in patients undergoing elective craniotomy for supratentorial tumors with the aid of skull pin head holder.

GENDER

Group	SEX		Total	p value by Chi sq test
	MALE	FEMALE		
DEXOMED	19 (63.33%)	11 (36.66%)	30 (100%)	0.405
LIGNOCAINE	22 (73.33%)	8 (26.66%)	30 (100%)	
Total	41 (68.33%)	19 (31.66%)	60 (100%)	



Results

While analysing gender status among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull pin head holder, it was observed that majority of the study subjects in dexmedetomidine group were males (n=19, 63.33%) and same status in lignocaine group (n=22, 73.33%) (p=0.405, chi squared test)

Discussion

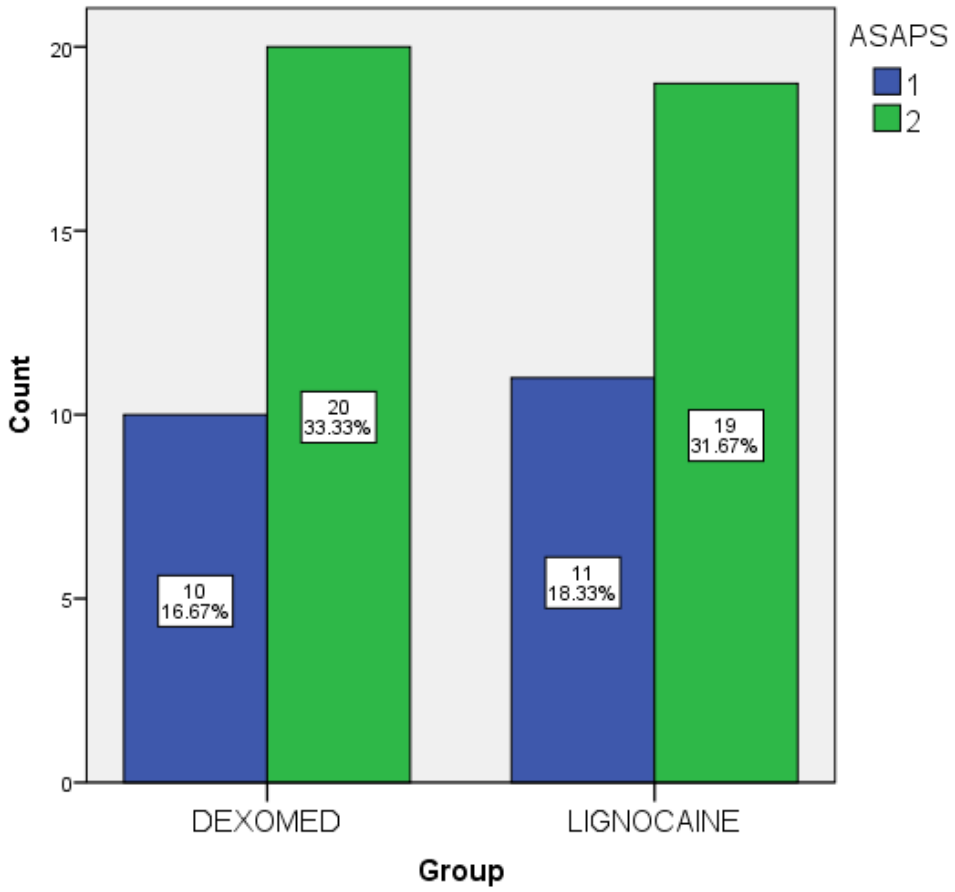
When statistically comparing gender status between the intervention groups, the difference in the percentage of male patients between dexmedetomidine group and lignocaine group (10%) was found to be statistically insignificant (p >0.05).

Conclusion

Gender of the study subjects is normally distributed across the intervention groups and has no effect on study outcomes in patients undergoing elective craniotomy for supratentorial tumors with the aid of skull pin head holder.

ASA PS

Group	ASA PS		Total	p value
	1	2		
DEXOMED	10 (33.33%)	20 (66.66%)	30 (100%)	0.786
LIGNOCAINE	11 (36.66%)	19 (63.33%)	30 (100%)	
Total	21 (35%)	39 (65%)	60 (100%)	



Results

While analysing ASA PS status among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull pin head holder, it was observed that majority of the study subjects in dexmedetomidine group were belonging to ASA PS II(n=20, 63.66%) and same status in lignocaine group (n=19, 63.33%) (p=0.786, chi squared test)

Discussion

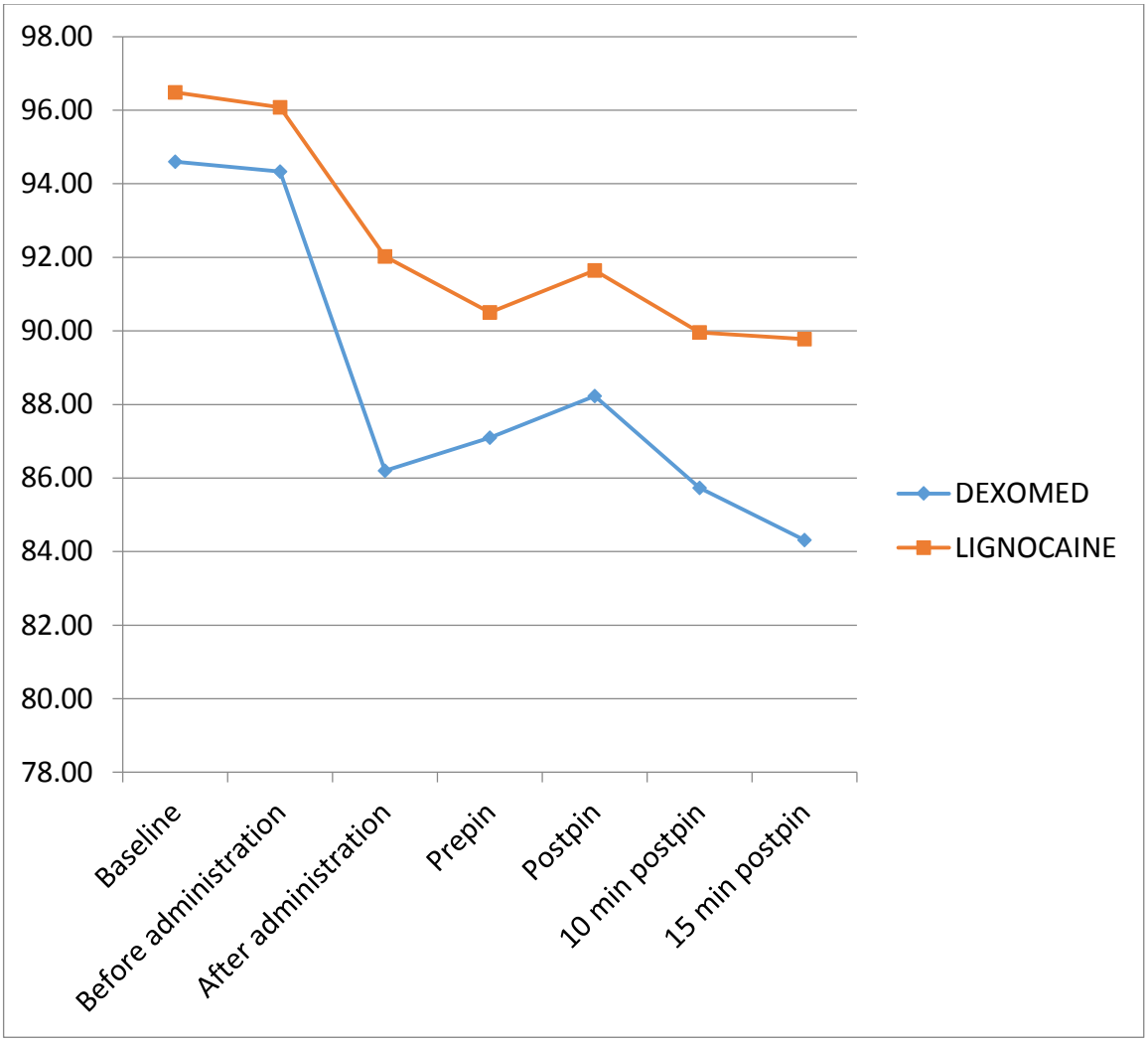
When statistically comparing ASA PS status between the intervention groups, the difference in the percentage of male patients between dexmedetomidine group and lignocaine group (0.33%) was found to be statistically insignificant (p >0.05).

Conclusion

Gender of the study subjects is normally distributed across the intervention groups and has no effect on study outcomes in patients undergoing elective craniotomy for supratentorial tumors with the aid of skull pin head holder.

HR

HR	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
Baseline(T1)	DEXOMED	30	80.97	5.25	0.924
	LIGNOCAINE	30	81.10	5.50	
Before administration of dexmed/local infiltration(T2)	DEXOMED	30	81.50	5.01	0.920
	LIGNOCAINE	30	81.63	5.26	
After administration of dexmed/local infiltration(T3)	DEXOMED	30	72.00	4.58	< 0.001
	LIGNOCAINE	30	77.00	5.19	
Prepin application(T4)	DEXOMED	30	71.87	4.11	< 0.001
	LIGNOCAINE	30	76.87	4.82	
Postpin application(T5)	DEXOMED	30	72.90	4.04	< 0.001
	LIGNOCAINE	30	77.87	4.71	
10 min postpin application(T10)	DEXOMED	30	72.37	3.55	0.001
	LIGNOCAINE	30	76.07	4.51	
15 min postpin application(T15)	DEXOMED	30	72.10	3.62	< 0.001
	LIGNOCAINE	30	76.40	3.94	



Results

While analysing the heart rate distribution among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull-pin head holder, it was observed that the attenuation of heart rate(HR) in the dexmedetomidine group was better when compared to the lignocaine group. Post pin application (T5) the mean heart rate for group dexmed was 72.90 and group lignocaine was 77.87(p=<0.001,unpaired t test)

Discussion

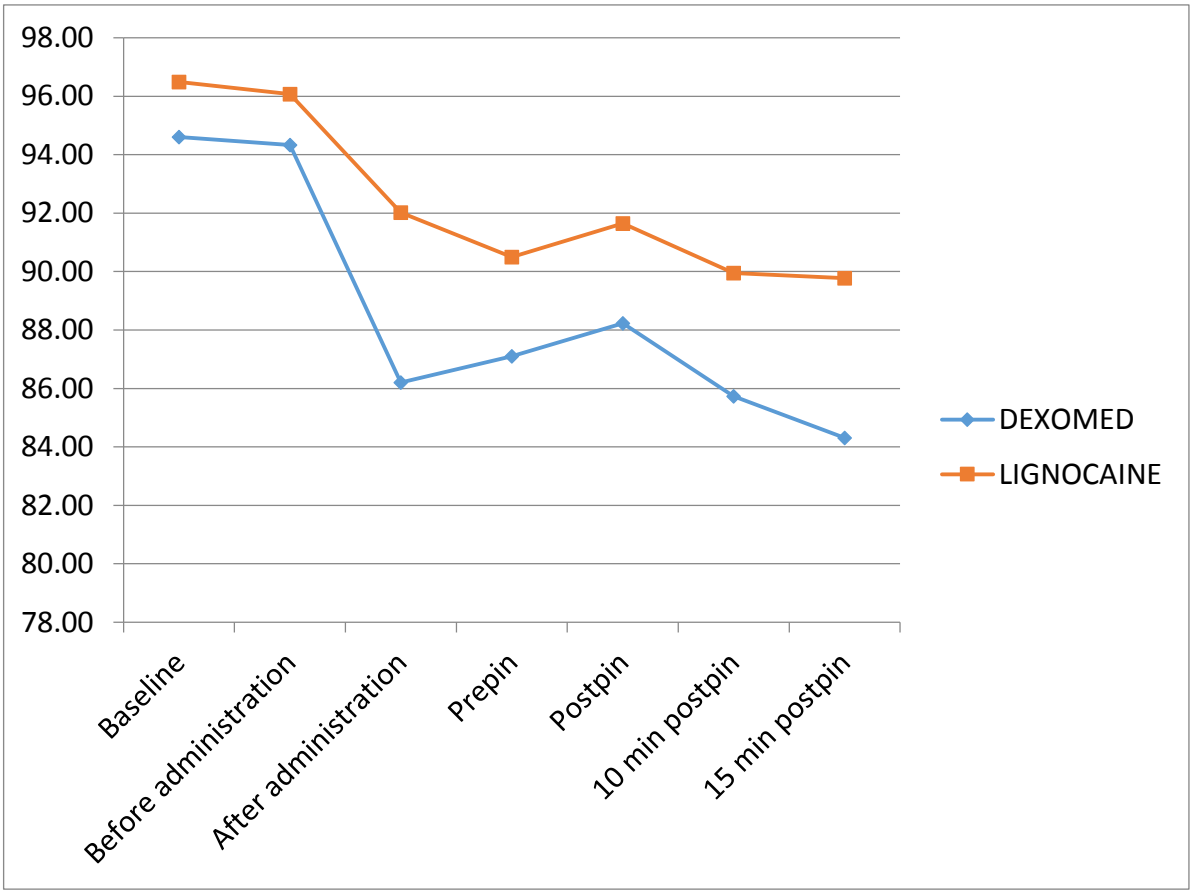
When statistically comparing the attenuation of heart rate(HR) between the intervention groups, the overall attenuation in the heart rate in the group dexmedetomidine is superior to group lignocaine. This trend of significantly lower heart rate in group dexmedetomidine when compared to lignocaine group was found to be statistically significant ($p < 0.05$).

Conclusion

Hence dexmedetomidine seems to be more advantageous than lignocaine in terms of attenuating HR(heart rate) associated with skull pin head holder application during elective craniotomies for supratentorial tumors.

SBP

SBP	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
Baseline(T1)	DEXOMED	30	125.60	9.39	0.748
	LIGNOCAINE	30	126.40	9.79	
Before administration of dexmed/local infiltration(T2)	DEXOMED	30	125.40	8.36	0.823
	LIGNOCAINE	30	125.90	8.90	
After administration of dexmed/local infiltration(T3)	DEXOMED	30	114.80	6.71	0.002
	LIGNOCAINE	30	121.00	7.95	
Prepin application(T4)	DEXOMED	30	115.70	6.92	0.084
	LIGNOCAINE	30	119.03	7.73	
Postpin application(T5)	DEXOMED	30	116.43	6.71	0.034
	LIGNOCAINE	30	120.40	7.38	
10 min postpin application(T10)	DEXOMED	30	113.10	6.02	0.005
	LIGNOCAINE	30	117.80	6.40	
15 min postpin application(T15)	DEXOMED	30	111.47	5.14	< 0.001
	LIGNOCAINE	30	117.20	5.90	



Results

While analysing the Systolic blood pressure (SBP) distribution among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull-pin head holder, it was observed that the attenuation of Systolic blood pressure in the dexmedetomidine group was better when compared to the lignocaine group. Post pin application (T5) the mean systolic blood pressure for group dexmedetomidine was 116.43 and group lignocaine was 120.40(p=<0.034, unpaired t test)

Discussion

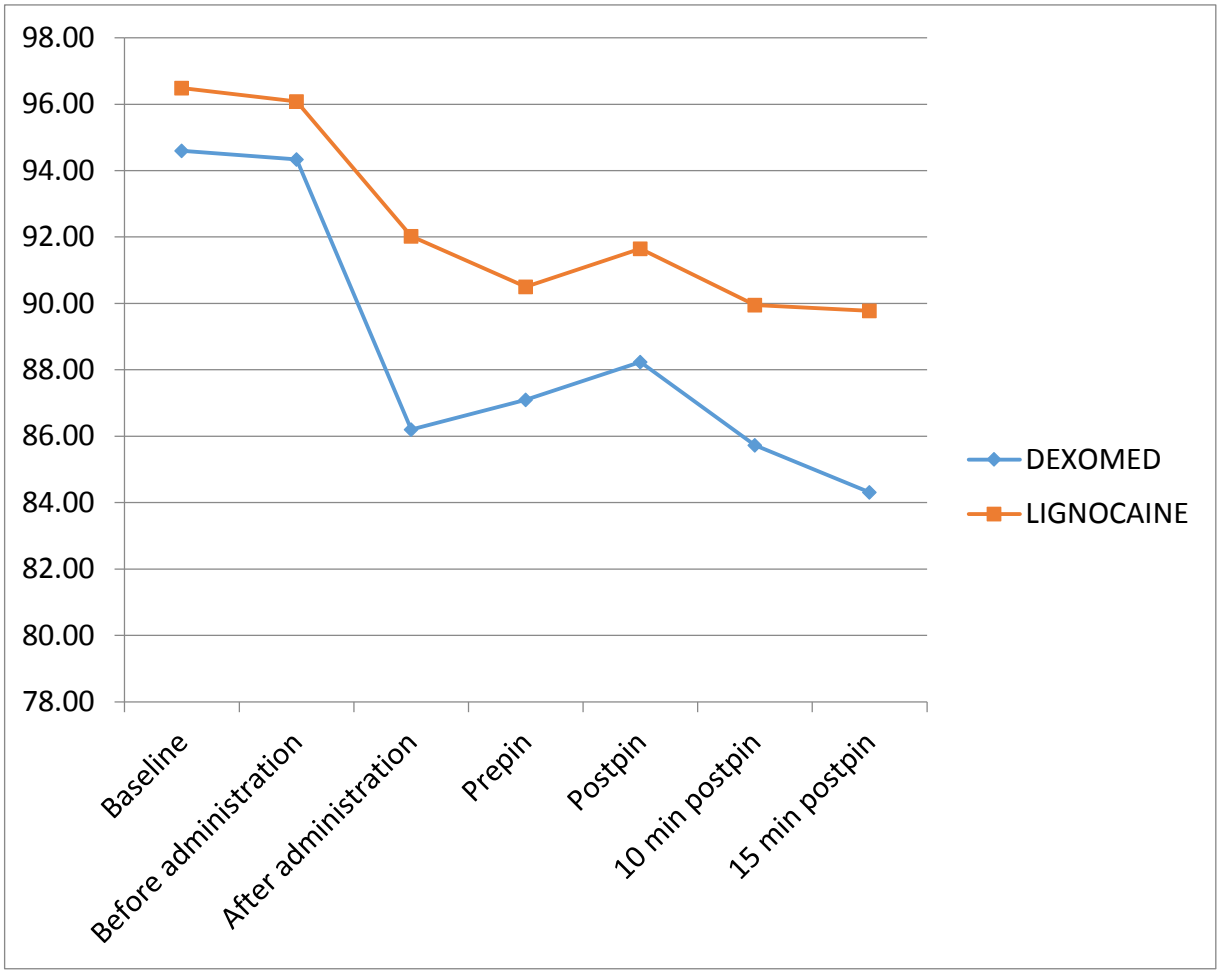
When statistically comparing the attenuation of Systolic blood pressure (SBP) between the intervention groups, the overall attenuation of SBP in the group dexmedetomidine is superior to group lignocaine. This trend of significantly lower systolic blood pressure in group dexmedetomidine when compared to lignocaine group was found to be statistically significant ($p < 0.05$).

Conclusion

Hence dexmedetomidine seems to be more advantageous than lignocaine in terms of attenuating Systolic blood pressure(SBP) associated with skull pin head holder application during elective craniotomies for supratentorial tumors.

DBP

DBP	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
Baseline(T1)	DEXOMED	30	79.10	6.21	0.157
	LIGNOCAINE	30	81.53	6.91	
Before administration of dexmed/local infiltration(T2)	DEXOMED	30	79.70	4.65	0.288
	LIGNOCAINE	30	81.17	5.87	
After administration of dexmed/local infiltration(T3)	DEXOMED	30	72.97	4.55	0.001
	LIGNOCAINE	30	77.53	5.48	
Prepin application(T4)	DEXOMED	30	72.80	4.48	0.012
	LIGNOCAINE	30	76.23	5.71	
Postpin application(T5)	DEXOMED	30	74.13	4.74	0.043
	LIGNOCAINE	30	76.93	5.70	
10 min postpin application(T10)	DEXOMED	30	72.20	4.85	0.005
	LIGNOCAINE	30	76.03	5.20	
15 min postpin application(T15)	DEXOMED	30	70.73	4.49	< 0.001
	LIGNOCAINE	30	76.07	4.73	



Results

While analysing the Diastolic blood pressure (DBP) distribution among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull-pin head holder, it was observed that the attenuation of Diastolic blood pressure in the dexmedetomidine group was better when compared to the lignocaine group. Post pin application (T5) the mean diastolic blood pressure for group dexmedetomidine was 74.13 and group lignocaine was 76.93(p=<0.043,unpaired t test)

Discussion

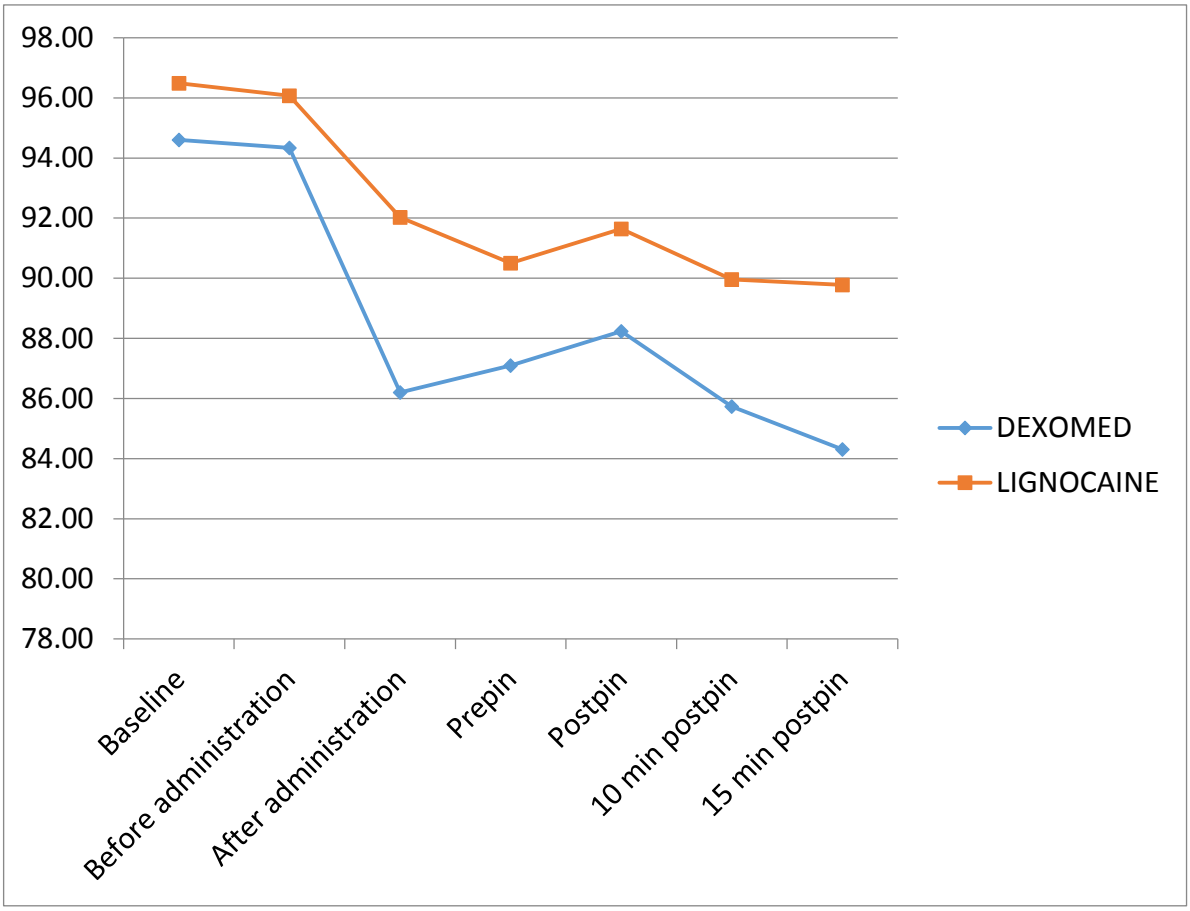
When statistically comparing the attenuation of Diastolic blood pressure (DBP) between the intervention groups, the overall attenuation of DBP in the group dexmedetomidine is superior to group lignocaine. This trend of significantly lower diastolic blood pressure in group dexmedetomidine when compared to lignocaine group was found to be statistically significant ($p < 0.05$).

Conclusion

Hence dexmedetomidine seems to be more advantageous than lignocaine in terms of attenuating Diastolic blood pressure (DBP) associated with skull pin head holder application during elective craniotomies for supratentorial tumors.

MAP

MAP	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
Baseline(T1)	DEXOMED	30	94.60	6.56	0.309
	LIGNOCAINE	30	96.49	7.64	
Before administration of dexmed/local infiltration (T2)	DEXOMED	30	94.33	5.54	0.273
	LIGNOCAINE	30	96.08	6.63	
After administration of dexmed/local infiltration (T3)	DEXOMED	30	86.20	4.79	< 0.001
	LIGNOCAINE	30	92.02	6.08	
Prepin application (T4)	DEXOMED	30	87.10	4.94	0.022
	LIGNOCAINE	30	90.50	6.16	
Postpin application (T5)	DEXOMED	30	88.23	4.96	0.017
	LIGNOCAINE	30	91.64	5.79	
10 min postpin application (T10)	DEXOMED	30	85.73	4.89	0.002
	LIGNOCAINE	30	89.96	5.29	
15 min postpin application (T15)	DEXOMED	30	84.31	4.11	< 0.001
	LIGNOCAINE	30	89.78	4.70	



Results

While analysing the Mean Arterial pressure (MAP) distribution among patients undergoing elective craniotomy for supratentorial tumors with the aid of skull-pin head holder, it was observed that the attenuation of Mean Arterial pressure in the dexmedetomidine group was better when compared to the lignocaine group. Post pin application (T5) the mean of mean arterial pressure (MAP) for group dexmedetomidine was 88.23 and group lignocaine was 91.64(p=<0.017,unpaired t test)

Discussion

When statistically comparing the attenuation of Mean Arterial pressure (MAP) between the intervention groups, the overall attenuation of MAP in the group dexmedetomidine is superior to group lignocaine. This trend of significantly lower Mean Arterial pressure in group dexmedetomidine when compared to lignocaine group was found to be statistically significant ($p < 0.05$).

Conclusion

Hence dexmedetomidine seems to be more advantageous than lignocaine in terms of attenuating Mean Arterial pressure(MAP) associated with skull pin head holder application during elective craniotomies for supratentorial tumors.

DISCUSSION

DISCUSSION

Different modalities have been experimented to reduce the haemodynamic response to skull pin application of which the most commonly studied method being local lignocaine infiltration at the pin application sites. However, this method was not always successful because of improper infiltration, changes in pin sites, head movement during fixation, and inadequate dosage of local anaesthetic.

This resulted in comparison of lignocaine infiltration with other modalities such as oral clonidine or gabapentin pre-medication, bupivacaine skull block, IV fentanyl and different IV anaesthetics. All the studies yielded varying results and thus it was identified that further research would be required to identify the ideal modality.

Dexmedetomidine, a selective alpha-2 Adrenoceptor agonist, has sedative, analgesic and anaesthetic-sparing effect. It decreases the HR, MAP and sympathetic nervous system activity. We compared dexmedetomidine with the commonly used method of local lignocaine infiltration at pin sites for attenuating the hemodynamic responses to skull pin insertion. Anaesthetic technique was standardized in this study.

Based on the standard recommended dose, group dexmedetomidine received 1mcg/kg of dexmedetomidine diluted to 10ml with 0.9% saline over 10 min at the time of induction. These patients received infiltration of the pin sites with 0.9% saline (3 ml at each site) to ensure blinding of the observer. Patients randomized to group lignocaine received 10 ml of 0.9% saline IV over 10 min at induction and then received infiltration of pin sites with 2% lignocaine 3ml at each site. The timing of dexmedetomidine infusion was such that the peak effect of the drug would concide with the time of pin application.

We found that HR and MAP were comparable between the groups at various time intervals in the study. Thus, it was observed that dexmedetomidine is more effective in controlling the haemodynamic response to skull pin application when compared to the usual method of local lignocaine infiltration. Despite dexmedetomidine having side effects such as hypotension and bradycardia which may be detrimental in a neurosurgical patient we did not observe any such side effects when dexmedetomidine was slowly infused over 10mins in the dose of 1mcg/kg.

The bradycardia/hypotension may not be attributable to dexmedetomidine in all the cases because occasionally the haemodynamic response to skull pin application can manifest as bradycardia/hypotension.

Few studies in literature have evaluated dexmedetomidine to control the haemodynamics during skull pin application. Uyar et.al. compared dexmedetomidine (1mcg/kg over 10 min) with placebo and its effect on haemodynamics during pin application. They found that dexmedetomidine attenuated the haemodynamic response to pin application. Contrary to the belief, they did not find hypotension and bradycardia requiring rescue medication in both the groups.

E1 Dawlatly et.al. also conducted a study in which 28 patients were randomized to four groups as Dex group (0.25..g/kg infusion of dexmedetomidine over 10 min), Ligno group (1% lignocaine infiltration at pin sites), Dex-Ligno group (combination of dexmedetomidine infusion and lignocaine infiltration) and placebo. They found that both dexmedetomidine and lignocaine were equally effective in attenuating the haemodynamic response to pin application.

The combination of low dose dexmedetomidine infusion and local lignocaine infiltration maximally attenuated the haemodynamic response. They, too, reported no hypotension and/or bradycardia requiring treatment.

Considering that both intravenous dexmedetomidine and local lignocaine infiltration attenuated hemodynamic responses to skull-pin head holder, we conclude that intravenous dexmedetomidine was a better option than local lignocaine in this regard as it attenuated and maintained stable hemodynamics throughout the surgery without causing deleterious side effects.

SUMMARY

SUMMARY

This study was done to compare the efficacy of intravenous injection of dexmedetomidine with local infiltration of lignocaine in attenuating the hemodynamic response accompanying MayField Skull-pin application in 60 patients divided into 2 groups.

Group D : i.v Dexmedetomidine 1mcg/kg over 10mins

Group L : 3ml of 2% local Lignocaine infiltration

60 ASA I and II patients aged 18 to 70 years undergoing elective craniotomy surgeries for supratentorial tumors under general anaesthesia were chosen for the study. After obtaining ethical committee approval the study population was chosen. Informed written consent was obtained from the patients. All patients were monitored with ECG, NIBP, pulse oximetry and EtCO2.

HR, NIBP, MAP was recorded starting from the baseline value(T1), pre-dexmed administration or pre-infiltration(T2), post-dexmed administration or post-infiltration(T3), pre-pin application(T4), post-pin application(T5), T10 (10minutes after pin application), T15(15minutes after pin application).

Dexmedetomidine is a highly selective and potent alpha 2 adrenoceptor agonist.

Lignocaine is a local anaesthetic acts by blocking the nerve conduction by decreasing the entry of sodium ions during upstroke of action potential. Minimal local irritant action and blocks sensory nerve endings, nerve trunks, neuromuscular junction, and ganglionic receptors.

In this study which was carried out in the Institute of Anaesthesiology and Critical care at RGGGH, Chennai we compared the efficacy of intravenous dexmedetomidine with local lignocaine in attenuating the hemodynamic response associated with May Field skull-pin head holder during craniotomy.

CONCLUSION

CONCLUSION

I conclude that intravenous dexmedetomidine (1mcg/kg given slowly over 10mins) is superior when compared with local infiltration of 2% lignocaine in attenuating the hemodynamic responses to skull pin head holder application during craniotomy.

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BIBLIOGRAPHY

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ANNEXURES

PROFORMA

TITLE: "PROSPECTIVE RANDOMISED COMPARITIVE STUDY BETWEEN INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER DURING CRANIOTOMY.

DATE: IP NO:

NAME:

AGE: SEX:

DIAGNOSIS:

SURGICAL PROCEDURE:

Ht: CVS: CNS:

Wt: RS:

PRE OP ASSESSMENT:

MMS:

HISTORY:

Any Co-morbid illness -

H/O Documented Difficult Airway-

H/O previous surgeries-

INFORMED CONSENT IN TAMIL:

RANDOMIZATION: Tick the following

1) GROUP D

2) GROUP L

IV line

PREMEDICATION

MONITORS

BASELINE VITAL PARAMETERS

Heart rate	
NIBP	
MAP	

Pre medication

Intubation

Intravenous /Infiltration

Pin application

OUTCOME MEASURES

Heart Rate (HR) and Mean Arterial Pressure (MAP) were recorded at the following time intervals.

- Pre- induction baseline (immediately before IV administration of dexmedetomidine)
- Pre-infiltration (just before infiltration of pin sites)
- Post- infiltration (just after infiltration of all pin sites)
- Pre-pin application (just before pin application)
- Post-pin application

at T1, T 2, T 3, T 4, T 5, T 10 and T15 minutes respectively after Pin insertion

EVENTS	HEART RATE (HR)	NIBP	MEAN ARTERIAL PRESSURE (MAP)
Pre- induction baseline (T1)			
Pre-infiltration (T2)			
Post- infiltration (T3)			
Pre-pin application (T4)			
Post-pin application (T5)			
10 Minutes after pin application ((T10)			
15 Minutes after pin application (T15)			

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.D.Aruna
I Year Post Graduate in Anaesthesiology
Institute of Anaesthesiology andCritical Care
Madras Medical College
Chennai 600 003

Dear Dr.D.Aruna,

The Institutional Ethics Committee has considered your request and approved your study titled **"PROSPECTIVE RANDOMISED COMPARITIVE STUDY BETWEEN INTRAVENOUS DEXMEDETOMEDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER APPLICATION DURING CRANIOTOMY " - NO.09072017**

The following members of Ethics Committee were present in the meeting hold on **07.07.2017** conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD.,	:Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., Dean, MMC,Ch-3	:Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	:Member Secretary
4. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3	: Member
5. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC	: Member
6. Prof.Shanthy Gunasingh, Director, Inst. of Social Obstetrics,KGH	: Member
7. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai	: Member
8. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3	: Member
9.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
10.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist
11.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

INFORMATION TO PARTICIPANTS

Investigator : Dr. ARUNA.D

Name of the Participant:

TITLE: "PROSPECTIVE RANDOMISED COMPARITIVE STUDY BETWEEN INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER DURING CRANIOTOMY.

You are invited to take part in this research study. We have got approval from the Institutional Ethical Committee. You are asked to participate because you satisfy the eligibility criteria .We want to compare between oral and Intravenous formulations of tranexamic acid and ethamsylate and study their effectiveness in reducing intra op and postoperative blood loss in patients undergoing cardiac valve replacement surgeries.

What is the Purpose of the Research:

To compare intravenous dexmedetomidine and local lignocaine to attenuate the hemodyamic resoponse to skull pin head holder during craniotomy.
1.To assess the hemodynamic response and stability to skull pin head holder.

The Study Design:

Total number of patients - 60

Group1- Group – D - Intravenous dexmedetomidine

Group2- Group – L -Local lignocaine

Benefits:

To attenuate the hemodynamic response to skull pin head holder during craniotomy, thereby preventing brain oedema, increased intracranial pressure or intracranial haemorrhage.

Discomforts and risks:

Hypotension and bradycardia.

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative, of setting the standard treatment and your safety is our prime concern.

Time :

Date : Signature / Thumb Impression of the patient

Place :

Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

PATIENT CONSENT FORM

Study title :

PROSPECTIVE RANDOMISED COMPARITIVE STUDY BETWEEN INTRAVENOUS DEXMEDETOMIDINE AND LOCAL LIGNOCAINE INFILTRATION TO ATTENUATE THE HEMODYNAMIC RESPONSE TO SKULL PIN HEAD HOLDER DURING CRANIOTOMY."

Study centre :

Institute of Anaesthesiology and Critical Care,
Rajiv Gandhi Govt. General Hospital,
Madras Medical College ,
Chennai- 600003

Participant name: **I.P. No:** **Age:** **Sex:**

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law . I agree not to restrict theuse of any data or results that arise from the study. I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological,biochemical,radiological tests.

I hereby agree to participate in this study.

Time:

Date: Signature / thumb impression of patient

Place:

Patient name:

Signature of the investigator:

Name of the investigator:

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சியாளர் பெயர் :

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சி தலைப்பு

கிரேனியாடமி அறுவை சிகிச்சையின் போது ஸ்கல் பிண் ஹேட் ஹோல்டர் போடும் பொழுது ஏற்படும் இரத்த அழுத்தம் மற்றும் நாடித்துடிப்பு காரணிகளை கட்டுப்படுத்துவதில் டெக்ஸ் மிடிடோமிடின் அல்லது லிக்னோகேயின் மருந்துகளில் சிறந்தது எது என ஒப்பிடுதல்.

ஆராய்ச்சியின் நோக்கம்

கிரேனியாடமி அறுவை சிகிச்சையின் போது ஸ்கல் பிண் ஹேட் ஹோல்டர் போடும் பொழுது ஏற்படும் இரத்த அழுத்தம் மற்றும் நாடித்துடிப்பு காரணிகளை கட்டுப்படுத்துவதில் டெக்ஸ் மிடிடோமிடின் அல்லது லிக்னோகேயின் மருந்துகளில் சிறந்தது எது என ஒப்பிட்டு பார்த்தல்.

- மருந்துகளின் பக்கவிளைவுகளை அறிதல்

ஆய்வின் தன்மை

ஆய்வில் பங்குபெறும் நோயாளிகள் இரண்டு குழுக்களாக பிரிக்கப்படுவர்.

குழு-1(குழு-D): இன்ட்ராவீனஸ் டெக்ஸ்மிடிடோமிடின் (1 மைக்ரோ கிராம்/கிலோ எடை 10 நிமிடங்களில்) செலுத்தப்படும்.

குழு-2(குழு-L): லோக்கல் லிக்னோகேயின் (2% 3மிலி பிண் போடுகின்ற இடத்தில்) செலுத்தப்படும்.

நன்மைகள்

கிரேனியாடமி அறுவை சிகிச்சையின் போது ஸ்கல் பிண் ஹேட் ஹோல்டர் போடும் பொழுது ஏற்படும் இரத்த அழுத்தம் மற்றும் நாடித்துடிப்பு மாறுதல்கள் சீராக்கப்படும்.

பக்க விளைவுகள்

மருந்து கொடுப்பதால் குறைந்த இரத்த அழுத்தம், குறைந்த நாடித்துடிப்பு ஏற்படலாம். அதற்கு மாற்று மருந்துகள் உடனடியாக கொடுக்கப்படும்.

இந்த முறையான ஆய்வு ஏற்கனவே பல இடங்களில் நடத்தப்பட்டுள்ளது. மேலும் இதன் பாதுகாப்பு உறுதிசெய்யப்பட்டுள்ளது. நீங்கள் இந்த ஆய்வில்

பங்குகொள்ள விரும்பவில்லை என்றால் எப்போதும் உபயோகிக்கப்படும் மருந்தே கொடுக்கப்படும். உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

இந்த ஆய்வு சம்பந்தமான எல்லா புள்ளி விவரங்கள் மற்றும் நோயாளிகளின் விவரங்கள் ரகசியமாக வைக்கப்படும். இந்த ஆய்வு சம்பந்தப்பட்ட எல்லா பரிசோதனைகள், மருந்துகள் மற்றும் மருத்துவ சேவைகள் அனைத்தும் நோயாளிகளுக்கு இலவசமாக வழங்கப்படும்.

ஆய்வாளரின் பெயர் **பங்குபெறுபவரின் பெயர்**

ஆய்வாளரின் கையொப்பம் **பங்குபெறுபவரின் கையொப்பம்**

<u>ஆராய்ச்சி ஒப்புதல் படிவம்</u>

ஆராயச்சியின் தலைப்பு

கிரேனியாடமி அறுவை சிகிச்சையின் போது ஸ்கல் பிண் ஹோட் ஹோல்டர் போடும் பொழுது ஏற்படும் இரத்த அழுத்தம் மற்றும் நாடித்துடிப்பு காரணிகளை கட்டுப்படுத்துவதில் டெக்ஸ் மிடிடோமிடின் அல்லது லிக்னோகேயின் மருந்துகளில் சிறந்தது எது என ஒப்பிடுதல்.

ஆய்வு நிலையம் : மயக்கவியல் துறை, சென்னை மருத்துவக் கல்லூரி சென்னை - 3.

பங்கு பெறுவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பங்குபெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் 'இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிகிறேன். ☐

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம்..... தேதி.....

ஆய்வாளரின் பெயர் .....

MASTER CHART - DEXMED

S.NO	NAME	AGE / SEX	ASA PS	T1 (BASELINE)			T2 (BEFORE ADMINISTRATION OF DEXMED)			T3 (AFTER ADMINISTRATION OF DEXMED)			T4 (PRE-PIN APPLICATION)			T5 (POST-PIN APPLICATION)			T10 (10 MINS AFTER PIN INSERTION)			T15 (15 MINS AFTER PIN INSERTION)		
				HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP
1	SAKTHIVEL	22/M	I	79	109/65	79.7	80	112/72	85.3	71	105/64	77.7	69	109/68	81.7	70	107/63	77.7	72	110/65	80	71	111/68	82.3
2	THIRAVIYAM	45/M	II	80	115/72	86.3	84	118/73	88.0	70	110/70	83.3	71	111/71	84.3	73	113/75	87.7	71	115/76	89	70	112/72	85.3
3	THILAGAVATHY	63/F	II	82	122/68	86.0	83	127/78	94.3	69	117/71	86.3	70	120/72	88.0	71	117/73	87.7	70	118/74	88.7	69	110/69	82.7
4	SHANMUGAM	53/M	II	85	134/72	92.7	87	132/75	94.0	77	121/70	87.0	75	119/75	89.7	78	117/74	88.3	77	115/73	87	76	112/70	84.0
5	RAMESH	35/M	I	82	118/75	89.3	81	124/80	94.7	74	112/72	85.3	73	113/72	85.7	74	115/74	87.7	75	111/76	87.7	75	110/71	84.0
6	KANNAGI	62/F	II	81	125/79	94.3	83	127/81	96.3	75	112/74	86.7	76	114/75	88.0	77	116/78	90.7	73	112/75	87.3	72	111/74	86.3
7	MUTHU	59/M	I	73	120/75	90.0	75	120/72	88.0	62	109/70	83.0	63	108/71	83.3	65	109/73	85.0	67	107/71	83	66	108/72	84.0
8	THAYALNAYAGI	49/F	II	85	119/75	89.7	84	121/76	91.0	73	111/67	81.7	72	113/65	81.0	73	112/67	82.0	71	108/64	78.7	69	105/65	78.3
9	GOVINDAMMAL	68/F	II	76	140/90	106.7	77	137/86	103.0	71	120/79	92.7	72	121/70	87.0	69	125/72	89.7	70	119/70	86.3	71	117/68	84.3
10	SIVA	32/M	I	79	111/73	85.7	78	114/75	88.0	69	106/65	78.7	70	105/63	77.0	71	109/65	79.7	67	104/67	79.3	68	105/62	76.3
11	ANANDHAN	55/M	II	71	131/85	100.3	72	129/83	98.3	60	114/72	86.0	61	117/70	85.7	63	118/72	87.3	65	111/68	82.3	67	109/66	80.3
12	VENKATESAN	47/M	II	75	128/79	95.3	77	127/80	95.7	70	122/78	92.7	69	119/77	91.0	71	119/77	91.0	72	114/75	88	70	110/72	84.7
13	PREM KUMAR	64/M	I	85	120/82	94.7	87	118/78	91.3	71	109/73	85.0	74	108/69	82.0	73	109/69	82.3	75	103/62	75.7	72	104/63	76.7
14	SARADHA	58/F	II	78	135/83	100.3	77	132/81	98.0	68	117/78	78.0	69	116/72	86.7	70	115/73	87.0	67	111/67	81.7	68	112/67	82.0
15	RANI	44/F	II	79	130/80	96.7	82	127/82	97.0	71	116/76	86.3	72	118/74	88.7	74	119/76	90.3	75	114/71	85.3	75	111/69	83.0
16	MANIKANDAN	57/M	II	80	124/84	97.3	81	121/83	95.7	70	112/77	88.7	71	111/78	89.0	73	113/80	91.0	72	110/79	89.3	74	109/79	89.0
17	KARUPPAIYAN	48/M	II	82	114/79	90.7	79	112/76	88.0	71	103/69	80.3	73	103/67	79.0	70	105/69	81.0	72	103/68	79.7	71	104/67	79.3
18	PUSHPA	69/F	II	86	130/82	98.0	85	129/83	98.3	77	120/75	90.0	76	121/76	91.0	75	123/75	91.0	74	120/73	88.7	73	117/70	85.7
19	LATHA	26/F	I	84	112/75	87.3	83	110/74	86.0	78	103/67	79.0	79	104/68	80.0	80	104/69	80.7	78	103/68	76.7	79	103/69	80.3
20	RAMASAMY	70/M	II	92	137/79	98.3	93	138/83	101.3	74	122/75	90.7	73	123/77	92.3	72	124/79	94.0	74	121/78	92.3	75	119/77	91.0
21	GOVINDARAJ	52/M	I	75	121/80	93.7	77	124/80	94.7	71	116/71	86.0	69	113/72	85.7	71	115/76	89.0	70	113/77	89	69	109/78	88.3
22	MAYAVAN	50/M	II	70	137/72	93.7	72	134/76	95.3	68	122/71	88.7	69	123/75	91.0	70	122/78	92.7	69	118/72	87.3	68	116/71	86.0
23	VELU	42/M	I	89	116/78	90.7	90	117/75	89.0	79	109/68	81.7	78	111/69	83.0	79	113/71	85.0	77	109/69	82.3	78	108/68	81.3
24	DHANABAL	74/M	II	82	140/90	106.7	83	138/89	105.3	77	123/79	93.7	78	125/78	93.7	80	126/79	94.7	79	121/77	91.7	78	119/76	90.3
25	KRISHNAVENI	38/F	I	79	127/86	99.7	78	124/86	98.7	69	112/81	91.3	70	114/80	91.3	72	116/81	92.7	71	112/79	90	70	111/78	89.0
26	POUNAMMAL	49/F	II	81	132/80	97.3	82	131/80	97.0	74	125/77	93.0	71	127/78	94.3	73	126/79	94.7	72	120/76	90.7	70	121/74	89.7
27	VELUSAMY	72/M	II	87	138/89	105.3	85	137/88	104.3	76	125/79	88.3	72	127/80	95.7	75	124/83	96.7	75	119/81	93.7	74	117/78	91.0
28	BALA	28/M	I	82	118/80	92.7	81	117/81	93.0	74	108/72	84.0	73	111/70	83.7	74	110/72	84.7	73	108/69	82	74	107/68	81.0
29	SUBRAMANI	59/M	II	90	139/87	104.3	90	138/85	84.7	81	124/78	93.3	79	127/79	95.0	80	129/77	94.3	78	125/75	91.7	79	121/72	88.3
30	CHELLAMAL	47/F	II	80	126/79	94.7	79	127/80	95.7	70	119/71	87.0	69	120/73	88.7	71	123/75	91.0	70	119/71	87	72	116/69	84.7

MASTER CHART - LIGNOCAINE

S.NO	NAME	AGE / SEX	ASA PS	T1 (BASELINE)			T2 (BEFORE LOCAL INFILTRATION OF LIGNOCAINE)			T3 (AFTER LOCAL INFILTRATION OF LIGNOCAINE)			T4 (PRE-PIN APPLICATION)			T5 (POST-PIN APPLICATION)			T10 (10 MINS AFTER PIN INSERTION)			T15 (15 MINS AFTER PIN INSERTION)		
				HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP	HR	NIBP	MAP
1	VENUGOPAL	40/M	I	78	116/74	88.0	81	117/76	89.7	77	112/72	85.3	76	110/71	84.0	77	112/70	84.0	76	111/71	84.3	78	110/70	83.3
2	PAPPAAMMAL	53/F	II	82	131/87	101.7	80	130/85	100.0	76	127/80	95.7	77	125/81	95.7	75	128/79	95.3	78	125/72	89.7	77	127/73	91.0
3	MADAVAN	32/M	II	77	121/81	94.3	79	123/84	97.0	74	119/81	93.7	73	118/80	92.7	75	121/83	95.7	74	118/80	92.7	73	119/81	93.7
4	PACHIAPPAN	49/M	II	87	138/87	104.0	88	135/86	102.3	85	131/82	98.3	86	132/80	97.3	83	131/80	97.0	82	127/78	94.3	82	124/79	94.0
5	UDAYAKUMAR	42/M	I	75	118/76	90.0	77	119/77	91.0	72	114/72	86.0	73	111/70	83.7	74	109/70	83.0	75	108/67	80.7	73	110/68	82.0
6	GOVINDARAJ	45/M	I	89	127/82	97.0	90	125/80	95.0	85	122/78	92.7	85	120/76	90.7	86	118/74	88.7	84	114/71	85.3	83	113/72	85.7
7	SUHASINI	21/F	I	75	110/67	81.3	80	112/68	82.7	77	109/65	79.7	76	105/63	77.0	75	109/65	79.7	74	106/67	80.0	76	107/69	81.7
8	VARADHAN	55/M	II	79	132/84	100.0	81	131/85	100.3	78	126/81	96.0	79	124/80	94.7	80	127/82	97.0	78	124/80	94.7	77	121/81	94.3
9	PACHAMUTHU	70/M	II	87	140/90	106.7	85	139/89	105.7	82	131/80	97.0	81	127/78	94.3	82	129/85	99.7	77	123/84	97.0	77	122/85	97.3
10	MARIMUTHU	61/M	II	81	129/86	100.3	83	130/85	100.0	79	123/81	95.0	80	120/80	93.3	83	123/79	93.7	79	119/77	91.0	78	120/75	90.0
11	SARAVANAN	35/M	II	82	135/83	100.3	81	132/81	98.0	75	126/79	94.7	76	122/78	92.7	78	124/79	94.0	76	120/80	93.3	78	116/81	92.7
12	SIVAKOLUNDHU	51/M	I	77	117/76	89.7	76	115/74	87.7	70	110/70	83.3	71	109/69	82.3	70	114/74	87.3	69	111/71	84.3	69	110/73	85.3
13	ARUMUGAM	63/M	II	84	127/83	97.7	83	125/81	95.7	78	119/80	93.0	77	119/78	91.7	79	121/79	93.0	77	116/78	90.7	79	117/79	91.7
14	MANI	69/M	II	83	137/86	103.0	82	138/85	102.7	76	131/82	98.3	75	129/80	96.3	77	133/82	99.0	75	127/80	95.7	77	125/81	95.7
15	VALLI	31/F	I	82	109/65	79.7	80	111/68	82.3	72	108/65	79.3	71	107/63	77.7	73	112/65	80.7	71	109/69	82.3	73	110/70	83.3
16	VARADARAJAN	59/M	II	82	120/81	94.0	81	121/83	95.7	77	118/79	92.0	76	117/77	90.3	77	118/78	91.3	76	117/79	91.7	77	115/78	90.3
17	MARIMUTHU	63/M	II	79	134/85	101.3	80	133/85	101.0	76	127/78	94.3	76	125/76	92.3	78	126/77	93.3	78	124/75	91.3	77	124/76	92.0
18	BHASKAR	29/M	I	70	117/72	87.0	72	119/75	89.7	68	112/73	86.0	69	113/73	86.3	70	115/71	85.7	69	113/70	84.3	71	115/71	85.7
19	PALANI	72/M	II	72	140/90	106.7	71	142/90	107.3	66	133/87	102.3	67	134/88	103.3	69	133/87	102.3	67	129/85	99.7	69	130/82	98.0
20	CHITRA	33/F	I	80	122/85	97.3	82	121/83	95.7	77	118/80	92.7	77	115/79	91.0	78	115/80	91.7	76	114/80	91.3	78	115/81	92.3
21	ESHWARI	28/F	I	85	111/69	83.0	87	112/70	84.0	82	109/68	81.7	80	108/68	81.3	80	110/70	83.3	79	109/69	82.3	80	110/70	83.3
22	MUNUSAMY	62/M	II	89	137/89	105.0	89	135/87	103.0	84	129/84	99.0	83	127/83	97.7	85	128/85	99.3	83	127/83	97.7	81	126/81	96.0
23	JEYARAMAN	35/M	I	75	114/75	88.0	73	113/76	88.3	69	110/72	84.7	69	109/70	83.0	70	110/69	89.3	66	111/69	83.0	67	113/70	84.3
24	MOHAN	44/M	II	92	123/86	98.3	90	122/84	96.7	85	118/80	92.7	83	117/78	91.0	84	119/79	92.3	81	115/78	90.3	80	116/75	88.7
25	GOMATHI	49/F	II	85	131/84	99.7	84	130/82	98.0	79	125/78	93.7	79	121/74	89.7	81	123/76	91.7	79	117/75	89.0	77	114/73	86.7
26	KRISHNASAMY	67/M	II	84	139/89	105.7	86	135/87	103.0	80	131/83	99.0	81	127/82	97.0	83	129/80	96.3	80	124/79	94.0	78	121/78	92.3
27	MAYILAMMAL	55/F	II	87	136/82	100.0	88	133/80	97.7	82	128/79	95.3	80	123/76	91.7	80	121/75	90.3	78	120/76	90.7	79	120/78	92.0
28	KUPPAN	38/M	I	71	119/78	91.7	72	121/79	93.0	70	117/76	89.7	71	116/77	90.0	73	115/75	88.3	70	118/77	90.7	71	115/74	87.7
29	NIRMALA	50/F	II	83	125/88	100.3	85	123/86	98.3	81	118/81	93.3	80	116/80	92.0	81	116/80	92.0	77	117/81	93.0	78	113/80	91.0
30	NOOKAN	52/M	II	81	137/86	103.0	83	135/84	101.0	78	129/80	96.3	79	125/79	94.3	80	123/80	94.3	78	121/80	93.7	79	118/78	91.3